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Resumen por el autor, Robert S. Ellis.

Normas para algunos cambios estructurales del cerebelo humano desde el nacimiento hasta la vejez.

En el recién nacido el cerebelo humano es relativamente pequeño comparado con el cerebro, pero crece rápidamente y a la edad de unos quince meses las partes del encéfalo adquieren aproximadamente los mismos pesos relativos del adulto. El peso relativo del cerebelo no varía de un modo significativo con la estatura, sexo, raza o inteligencia. Entre el nacimiento y la edad de quince meses la capa celular de los granos externos desaparece, las células de Purkinje crecen hasta alcanzar el tamaño normal del adulto, las capas molecular y granulosa interna adquieren la misma anchura relativa de las del adulto y las vainas de mielina crecen rápidamente, especialmente al final de este periodo. Estos cambios deben relacionarse con el hecho de que próximamente en este tiempo la actividad motriz del niño aumenta progresivamente y está comenzando a andar. Con el principio de la senescencia coincide una pérdida de células de Purkinje y una pérdida resultante de fibras mielinadas. Con este cambio estructural debe relacionarse la pérdida de fuerza y coordinación muscular, tan característica de la vejez. Existen algunas pruebas de que durante la vejez el hemisferio cerebelar derecho pierde mas células que el izquierdo, a causa tal vez de los efectos del uso excesivo de la mitad derecha del cuerpo. En los casos estudiados se ha encontrado menor número de células de Purkinje en los cerebelos de las hembras que en los de los varones.

Translation by José F. Nonidez
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NORMS FOR SOME STRUCTURAL CHANGES IN THE HUMAN CEREBELLUM FROM BIRTH TO OLD AGE

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EIGHT CHARTS

In a previous paper (Ellis, '19) I reported the results of a quantitative study of the Purkinje cells in normal, subnormal, and senescent human cerebella; the variations in the number of these cells in different cerebella were correlated with differences in muscular strength and in the development of motor coordination. However, the results presented for the decrease in the number of Purkinje cells with advancing age were based on such a small number of cases that it seemed desirable to extend the observations and to determine with more certainty the accuracy of some of the conclusions reached. This has been done, and the results of the further study are presented in this paper. In addition, I have reviewed the literature on the growth of the human cerebellum, have added some original observations, and have attempted to give a résumé of some important normal—not pathological—structural changes in the cerebellum from birth to death in old age. Variations from the norm have been observed, and as far as possible these structural changes have been correlated with changes in motor efficiency.

For the increase in the weight of the cerebellum during growth I have used the results of Boyd ('61), Danielbako' ('85), and Pfister ('97-'03); on the significance of the relative weight of the cerebellum I have reviewed the work of Gall (1807), Leuret ('39), Hatai ('15), Marshall ('92), Bischoff ('80), Meynert ('67), Weisbach ('66-'67), and Spitzka ('07), and I have calculated the relative weights of 152 cerebella from data given by Mall ('09) and by Bean ('06), and to this I have added the relative weights of

the cerebella of eighteen idiots and imbeciles whose brains are in The Wistar Institute Museum. On the disappearance of the layer of external granule cells I have reviewed the work of Vignal ('89), Berliner ('05), Biach ('09), Löwy ('10), Takasu ('05) and Addison ('11), and I have verified their conclusions by a study of a number of cases of human cerebella. For the relative thicknesses of the molecular, internal granular, and fiber layers, I have reviewed the work of Engel ('63), Krohn ('92), and Roncoroni ('05) and I have added some original measurements. Material for satisfactory measurements of the growth in size of the Purkinje cells has not been available, but I have made a few measurements on such cases as I could obtain. I have counted the Purkinje cells in two areas of both hemispheres of sixty-three cerebella from negroes, whites, and mulattoes of both sexes and of ages ranging from twelve to ninety-two years, and have compared these results with those already reported. On the growth and degeneration of the myelin sheath I have reviewed the work of Engel ('63), Lui ('94), de Sanctis ('98), Berliner ('05) and Löwy ('10).

Finally I have studied the degeneration of the cells of the dentate nucleus in senescence.

Many of the papers discussed are, it is true, rather old, but I have felt justified in bringing these various data together in order to get a general view of the different changes in the cerebellum during life and of the relation of these to variations in functional efficiency.

THE WEIGHT OF THE CEREBELLUM

Perfectly satisfactory weights for the human cerebellum during the early stages of growth are not available, and hospital material probably gives results which are below the average for the population at large. It is consequently not surprising that the weights recorded by different observers show more or less variation.

Boyd, in England, made extensive records of the weights of the parts of the brain, as well as of other organs, and these have been compiled and published by Sharpey ('61), and by Marshall

('92). Table 1 gives the weights of the cerebellum from birth to twenty years of age together with the percentage which the cerebellum is of the encephalon. These are in ounces in the original tables, but I have taken the liberty of converting them into grams for the sake of comparison with other results.

The body weights listed by Boyd show that the infants autopsied were much underdeveloped, and it is probable that the brain weights for the period of infancy are below normal.

A somewhat more satisfactory series of weights for the period of growth has been made by Pfister, in Berlin ('97-'03). Instead of taking all the cases that came to hand, he has been careful to reject all the brains that were underdeveloped, oedematous, anaemic, or pathological in any way that would appreciably affect the gross weight. His results are presented with Boyd's in table 1.

As the weights given by Boyd and Pfister naturally show some variation, I have attempted to determine the normal curve for the growth in weight of the cerebellum and for the encephalon as a whole during the first two years. This is shown in chart 1. The method used was as follows: The weights given by Boyd, Danielbekof (not given in table 1), and Pfister were plotted, and smooth graphs for the combined data were drawn so as to represent as nearly as possible the recorded weights. The graphs thus drawn are intended to show the normal relation between the weights of the encephalon and the cerebellum in both sexes, and from these graphs it is possible to determine the normal weights for either sex at any age less than two years. A series of values determined in this manner is given in table 2.

In both the chart and table I have made the relative weights of the cerebellum in males and females the same. It seems, however, not improbable that in females there may be some precocity and that consequently during early growth the relative weight of the female cerebellum may be somewhat higher than that of the male. The results of Pfister especially, and of Danielbekof also, would at least agree very well with this view, although they do not prove it.

TABLE I

The increase in the weight of the cerebellum after birth

BOYD						PFISTER					
Age	Sex	Encephalon	Cerebellum	Percentage weight of cerebellum	Number of cases	Age	Sex	Encephalon	Cerebellum	Percentage weight of cerebellum	Number of cases
0 (birth)	♂	331	20	5.9	45	2-4 wks.	♂	431	28	6.0	17
	♀	284	18	6.2	45		♀	396	24	6.0	13
1-3 mos.	♂	495	30	6.1	16	2 mos.	♂	461	31	6.7	10
	♀	453	26	5.6	22		♀	415	29	6.7	6
4-6 mos.	♂	605	49	8.1	15	3 mos.	♂	519	41	7.8	10
	♀	561	48	8.6	25		♀	504	39	7.9	11
7-12 mos.	♂	779	78	10.0	45	4-5 mos.	♂	583	45	7.9	8
	♀	730	66	9.0	45		♀	562	50	8.9	19
2 yrs.	♂	944	101	10.6	34	6-8 mos.	♂	733	72	9.0	12
	♀	846	90	10.6	33		♀	666	65	9.5	14
3-4 yrs.	♂	1099	114	10.4	28	9-10 mos.	♂	786	81	10.0	6
	♀	993	105	10.6	28		♀	684	67	10.0	8
5-7 yrs.	♂	1143	118	10.4	26	11-12 mos.	♂	851	85	10.0	5
	♀	1139	119	10.4	23		♀	727	69	10.8	2
8-14 yrs.	♂	1305	138	10.5	19	13-18 mos.	♂	944 ¹	100	10.6	11
	♀	1158	121	10.5	18		♀	873 ¹	96	11.0	6
15-20 yrs.	♂	1379	151	11.0	17	19-24 mos.	♂	1082 ¹	119	11.0	4
	♀	1248	132	10.6	14		♀	965 ¹	109	11.3	4
	♂					3-4 yrs.	♂	1136 ¹	125	11.0	16
	♀						♀	1035 ¹	117	11.3	12
	♂					5-8 yrs.	♂	1200 ¹	132	11.0	15
	♀						♀	1116 ¹	125	11.2	8
	♂					11-14 yrs.	♂	1245 ¹	137	11.0	7
	♀						♀	1191 ¹	131	11.0	3

¹ Estimated values calculated from the absolute and percentage weights of the cerebellum as given by Pfister.

Table 2 shows that at birth the cerebellum is very small and underdeveloped, being only about 5.7 per cent of the total brain weight, while in the adult it has nearly double that percentage. During the first year the cerebellum grows with great rapidity, so that by the end of that time it has reached nearly two-thirds its adult weight; by the end of the second year it has four-fifths

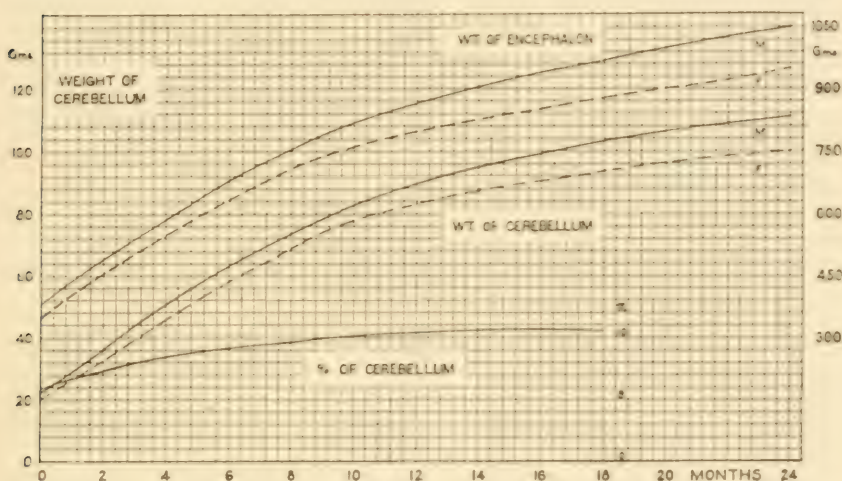


Chart 1 Graphs for the growth of the human encephalon and cerebellum during the first twenty-four months of life. The ordinate values differ for the three records. On the ordinate at the left are the values for the weight of the cerebellum: to the right for the weight of the cerebrum, and within the chart, at the right, for the percentage weight of the cerebellum. The weight of the encephalon is shown by the upper graphs: males; females. The weight of the cerebellum is shown by the middle graphs: males; females. The percentage weight of the cerebellum is given for the first eighteen months by the lowest graph, without distinction of sex. All the graphs have been smoothed.

of its adult weight and the period of rapid growth is over. This appears clearly from chart 1.

As a result of its rapid growth, the cerebellum gains steadily on the cerebral hemispheres until the tenth to twelfth months by which time it has reached approximately its relative weight in the adult. No very marked change in this relative weight is found after the first year.

The absolute and relative weights of the cerebellum for the ages of twenty to ninety years are given in table 3, which is based on the table of weights compiled by Sharpey from Boyd's records.

TABLE 2

This table gives the weights of the encephalon and of the cerebellum as read from the smoothed graphs, based on the observed weights given by Boyd, Danielbekof, and Pfister

AGE	SEX	ENCEPHALON	CEREBELLUM	PERCENTAGE WEIGHT OF CEREBELLUM
<i>months</i>				
0 (birth)	♂	385	22	5.7
	♀	350	20	5.7
2	♂	490	36	7.4
	♀	452	33	7.4
4	♂	585	50	8.5
	♀	545	46	8.5
6	♂	690	63	9.2
	♀	635	58	9.2
9	♂	790	79	10.0
	♀	730	73	10.0
12	♂	860	89	10.4
	♀	795	83	10.4
18	♂	970	103	10.6
	♀	875	93	10.6
24	♂	1055	112	10.6
	♀	950	101	10.6

The variations in the absolute weight of the cerebellum, according to Pfister, amount to as much as 10 grams in the first month, 20 grams in the second month, and 30 grams or more in the third month and thereafter. The variations in the cerebrum are likewise great, but there does not appear to be any constant relation between these variations; Pfister does not find it possible

to explain them in terms of body length and weight. At times the encephalon is above weight and the cerebellum below weight, or vice versa; in other cases the encephalon is above or below weight, but the parts are proportionately developed. Chart 2 shows the range of some of these variations, accompanied by the absolute weights of the parts of the brain.

TABLE 3

This table shows the absolute weights of the encephalon and the cerebellum and the percentage weight of the cerebellum with advancing years. Based on Boyd's results as compiled by Sharpey

AGE	SEX	ENCEPHALON	CEREBELLUM	PERCENTAGE WEIGHT OF CEREBELLUM	NUMBER OF CASES
<i>years</i>					
20-30	♂	1360	147	10.8	55
	♀	1241	137	11.0	70
30-40	♂	1369	146	10.7	103
	♀	1224	135	11.0	85
40-50	♂	1356	149	10.9	135
	♀	1216	133	11.0	97
50-60	♂	1347	146	10.8	110
	♀	1225	131	10.7	100
60-70	♂	1318	141	10.7	123
	♀	1213	133	11.0	142
70-80	♂	1292	141	10.9	102
	♀	1172	127	10.8	146
80	♂	1286	136	10.6	24
	♀	1130	127	11.2	75

Pfister states that the relative weight of the cerebellum varies as much as 2 per cent, by which he means presumably that at birth the relative weight would range between 4.7 and 6.7 per cent of the weight of the encephalon, with a similar range of variation for successive periods. My own results based on several groups of cases show that 50 per cent of adult cerebella have

weights which are between 9.8 and 11.8 per cent of the weight of the encephalon. The extreme range of relative weights for a given weight of the encephalon, as far as my experience goes, is illustrated by the two pathological cases shown in table 4.

The first case is half of the relative weight for the age of forty days, the normal being about 6.7 per cent; the second case is more than double the average relative weight for the adult, which

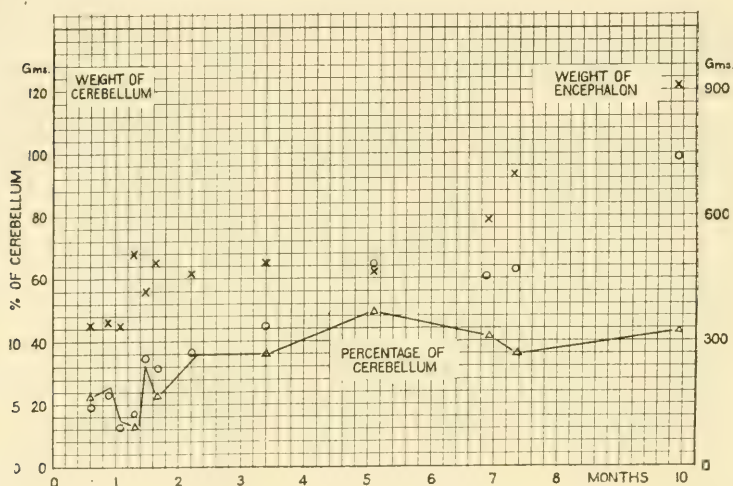


Chart 2 Showing the variations in the weights of the human encephalon and of the cerebellum—both sexes—together with the percentage weights of the cerebellum, during the first ten months of life. The ordinates for the percentage weight of the cerebellum Δ — Δ stand at the extreme left. The ordinates for the weight of the cerebellum O O on the left side just to the right of the foregoing. The ordinates for the weight of the encephalon X X to the right.

TABLE 4

Two extreme variations in relative weight of the cerebellum (pathological)

NUMBER	AGE	WEIGHT OF ENCEPHALON	WEIGHT OF CEREBELLUM	PERCENTAGE WEIGHT OF CEREBELLUM
		grams	grams	
E1	40 days	510	17	3.3
E3	21 years	505	118	23.4

is about 10.8 per cent. It is hardly necessary to add that cases such as these two are very rare. They are to be regarded as due to pathological arrest of development either of the cerebellum or of the cerebrum. The range of relative weights ordinarily found is shown in chart 3.

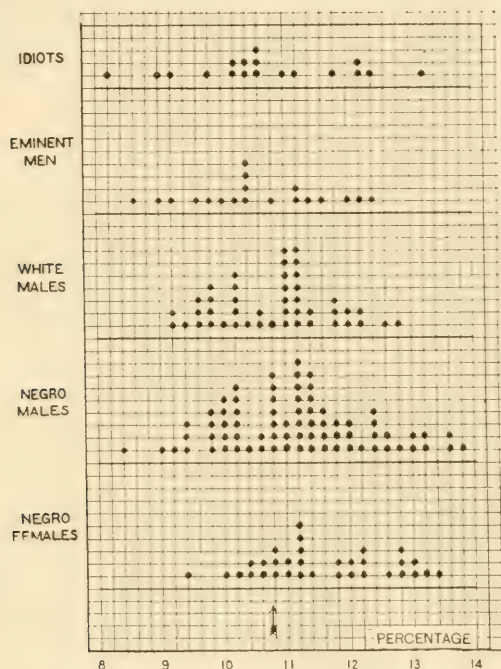


Chart 3 Giving the frequencies of the percentage weights of the cerebellum in five groups of human brains: 18 idiots and imbeciles; 19 eminent men; 45 ordinary white males; 74 negro males; 33 negro females.

The significance of the relative size of the cerebellum has received a great deal of attention since the days of Gall (1807). His view that it was connected with the sex instinct is well known. Leuret ('39) criticised this theory, and in support of his position he presented the weights of the encephalon and cerebellum in stallions, geldings, and mares; from his results I have arranged table 5.

The values given in the table do not seem to indicate a positive correlation between reproductive activity and the relative weight of the cerebellum, but they do seem to indicate a negative one, which would be quite as hard to understand. To throw any light possible on the question, I studied the weights of the parts of the brain in the male albino rat after castration. The data for this purpose were kindly offered me by Doctor Hatai, and for the details of the experiment the reader is referred to his paper ('15). From his results I have arranged table 6.

TABLE 5

The relative weight of the cerebellum in stallions, geldings and mares (after Leuret)

	NUMBER OF CASES	WEIGHT OF ENCEPHALON	WEIGHT OF CEREBELLUM	PERCENTAGE WEIGHT OF CEREBELLUM
		<i>grams</i>	<i>grams</i>	
Stallions.....	10	534	61	11.4
Geldings.....	21	520	70	13.5
Mares.....	12	498	61	12.2

TABLE 6

The effect of gonadectomy on the relative weights of the parts of the brain of the albino rat based on the work of Hatai, 1915

NUMBER OF CASES	GROUP	PERCENTAGE WEIGHT OF THE PARTS OF THE ENCEPHALON			
		Cerebrum	Cerebellum	Olfactory bulb	Stem
20	Castrated	62.9	14.7	3.2	19.2
20	Control	62.1	14.7	3.8	19.4

As will be observed from the table, there is no change in the relative weight of the cerebellum of the male albino rat as a result of gonadectomy. In view of the relations in the rat, interpretation of the figures given by Leuret for horses is not easy, but at least it seems clear that his results do not agree with any of the theories so far advanced.

In this connection it is desirable to examine the view of Marshall ('92), who concludes, on the basis of his excellent classification of Boyd's results, that the cerebellum is relatively heavier

in females than in males. From his table I have arranged table 7, which shows the variations in both absolute and relative weights in both sexes of different statures for the three decades from twenty to fifty years—the most active period of adult life when any differences due to sex or stature should be most evident, if present at all.

TABLE 7

The weight of the cerebellum according to age, sex, and stature. Based on Marshall's tables

AGE	HEIGHT, INCHES 69 PLUS 64 PLUS				HEIGHT, INCHES 66-68 61-63				HEIGHT, INCHES 65- 60-					
	Sex	Number of cases	Weight of cerebellum	Percentage weight of cerebellum	Sex	Number of cases	Weight of cerebellum	Percentage weight of cerebellum	Sex	Number of cases	Weight of cerebellum	Percentage weight of cerebellum	Average percentage weight for each age group	
<i>years</i>														
20-30	♂	14	145	10.6	♂	23	151	10.8	♂	15	148	11.3	10.9	
	♀	18	133	10.6	♀	32	139	11.5	♀	12	133	11.3	11.1	
30-40	♂	23	153	10.7	♂	48	142	10.5	♂	23	133	10.0	10.4	
	♀	26	133	10.5	♀	30	136	11.1	♀	15	131	10.7	10.7	
40-50	♂	28	148	10.7	♂	56	148	10.9	♂	32	145	11.0	10.9	
	♀	32	131	10.8	♀	35	131	10.7	♀	14	133	10.9	10.8	
Average				10.65					10.92				10.87	
Average for all cases, both sexes.....													10.82	

An examination of the table shows that his conclusion is open to question. The percentage weights of the cerebellum for females are not uniformly higher than for males—to be exact, they are higher in five groups out of nine in the table; in three groups the values for males are higher, and in one group the values for the sexes are the same. Under such conditions, the fact that the average percentage weight of the cerebellum is very slightly higher for females than for males can hardly be regarded in itself as significant.

The figures given by other observers serve only to strengthen the conclusion that there is no adult sex difference in the relative weight of the cerebellum. Bischoff ('80) gives the percentage weight of the 'Kleinhirn' for German males as 12.9 and for German females as 12.8; as his 'Kleinhirn' includes the brain stem, it means percentage weights for the cerebellum of about 10.9 and 10.8, respectively. Meynert ('67-'68) gives values of 11.2 and 11.3 for males and females, respectively. Weisbach ('66-'67) reports the percentage weight of the cerebellum to be less in Slavic males than in Slavic females, the values being 10.7 and 11.0, respectively, while among the South Germans the corresponding values are given as 10.8 (males) and 10.6 (females). No real difference between the sexes is apparent from these figures, and similar results could be given from some other authors without showing any preponderance of evidence on either side.

Chart 3, to be referred to later, shows the relative weights of the cerebellum in seventy-four male and thirty-three female negroes. This chart might be taken to indicate a relatively larger cerebellum in females of that race, but the number of cases is too small to be conclusive.

In my opinion, the evidence at hand is so well balanced that we are not safe in assuming for man any difference in the relative weights of the cerebellum in males and females at maturity, although, as has been pointed out, the female cerebellum may be somewhat precocious in its growth and so may be relatively heavier than that of the male during early life.

The relation of the relative weight of the cerebellum to stature has been examined by Weisbach (op. cit.), and by Marshall (op. cit.). Both agree that as stature increases the relative weight of the cerebellum increases also. If, however, we return to table 7, which, I believe, contains the best available data on the subject, we find, if anything, a lower relative weight of the cerebellum in tall persons. But the average differences are so small and the variations in the values for individual groups are relatively so great that no real significance can be attached to the differences found. We may then, I think, safely disregard Marshall's conclusion as to the effect of stature on the relative weight of the cerebellum.

The relative weight of the cerebellum according to the grade of the intelligence has been studied by Spitzka ('07), who gives a table showing the ratio of the weights of the cerebellum to the weights of the cerebrum in ten ordinary and eleven eminent men, and from this he concludes:

"A glance at the list shows that while in ordinary men the ratios cluster around 1:7.5, among eminent men it is fully a unit higher; that is to say, the cerebrum, or essential-thought apparatus, is relatively more massive, while the somatic organ of motor co-ordination (cerebellum) remains relatively reduced" (p. 300). This sounds very plausible, but let us examine the matter more closely. According to the weights given by Boyd for English males, the average weight of the cerebellum is about 148 grams and the average weight of the cerebrum is close to 1200 grams. Bischoff reports approximately the same figures for German and for French males. On this basis, then, the ratio for ordinary men should be 1:8 instead of 1:7.5, as Spitzka has it; so the superiority of the eminent men is reduced by half. To clear the matter up still further, I tabulated all the cases of eminent men reported by Spitzka, in which the percentage weight of the cerebellum could be determined. These are nineteen in number. I then weighed the parts of the encephalon of eighteen idiots and imbeciles, these, with one exception (table 4), being all of the brains of this class that were available in The Wistar Institute Museum. The results are presented in table 8 and in chart 3.

A glance at the chart and a comparison of the distribution of the percentage values in the different types of cases shows clearly that the number of cases is too small to show exactly the normal probability curve; at the same time, it leaves little room for doubt that the relative weights of the parts of the encephalon do not show significant variations corresponding to different levels of intelligence.

The foregoing conclusion is another reason for doubting the existence of a sex difference in relative cerebellar weight, a difference which has been often connected with a supposed difference in intelligence between males and females.

The problem as to whether there are racial differences in relative weight of the cerebellum has not been adequately studied. However, I have attempted to throw some light on the subject by comparing the cerebella of whites and negroes.

As I have not been able to secure a large number of fresh negro brains for the study of this point, I have had recourse to data given by Mall ('09). Unfortunately, for my purposes at least,

TABLE 8

The relative weights of the cerebellum in eminent men and in idiots and imbeciles

EMINENT MEN, BASED ON DATA FROM SPITZKA ('07)	PERCENTAGE WEIGHT OF CEREBELLUM	IDIOTS AND IMBECILES W. I. NO.	PERCENTAGE WEIGHT OF CEREBELLUM
Pepper, Wm.	8.6	E15	8.3
Letourneau, Chas.	9.1	15310	9.1
Seguin, E. C.	9.3	14942	9.3
Leidy, Jos.	9.7	14880	9.8
Seguin, Edouard	9.8	15145	10.2
Train, G. F.	10.0	15144	10.3
Bertillion, Adolphe	10.2	15113	10.5
Giacomini, Carlo	10.4	15111	10.5
Powell, J. W.	10.4	15320	10.6
Curtice, Hosea	10.4	15298	10.6
Cuvier, Geo. L. C.	10.5	15249	10.7
Pond, J. B.	10.9	15194	11.0
Jeffrey, Lord F.	11.3	15252	11.2
Webster, Daniel	11.3	15122	11.9
Leidy, Philip	11.5	15250	12.2
Fuchs, Konrad H.	11.7	15299	12.2
Coudereau, Auguste	12.1	15214	12.4
Cope, E. D.	12.3	15297	13.3
Allen, Harrison	12.4		
Averages.....	10.63		10.77

he does not give the weights of the parts of the brain when fresh, but after fixation. Also he gives the weight of the cerebellum combined with the brain stem. This makes the problem more complex, but I believe I have secured satisfactory and comparable results by resorting to the following procedure:

The brain stem is nearly always approximately 2 per cent of the weight of the encephalon; I have accordingly deducted this amount from the weight given for the combined cerebellum and

stem. This gives, with but little error, the weight of the cerebellum alone. From this value I calculated the percentage which the cerebellum is of the encephalon. There remains, however, the question as to the effect of fixation and preservation in formalin on the relative weight of the parts of the brain. According to Donaldson ('94), bichromate changes slightly the relative weights of the parts of the encephalon, so it seems probable that formalin may have a similar effect. I attempted to estimate this effect in two ways. First, I weighed again ten of the brains used by Mall and compared the changes in relative weight of the parts. Five showed increases in relative weight of the cerebellum and stem amounting on an average to 0.2 per cent, that is an increase from 11 per cent to 11.2 per cent, and five showed decreases in relative weight which averaged 0.4 per cent. The maximum change in any case was a loss of 0.5 per cent. Second, I plotted the percentage weights of the cerebellum on the per cent losses in absolute weight of the encephalon to see whether the group would give any consistent curve showing either loss or gain in percentage weight of the cerebellum with loss in weight of the encephalon.

I did this both for the negro brains and for the white ones included in Mall's study. The values for the white males gave a uniformly rising curve indicating a gain in percentage weight of the cerebellum with loss in weight of the encephalon; the values for the negro males did not give a very good curve, but indicated the same tendency as that for the white males; the values for negro females were distributed in such a manner that it was impossible to draw a conclusion.

The changes in the weight of the encephalon during fixation and preservation depend, as Pfister has pointed out ('03), on its condition at the time of fixation, and as the condition of different brains varies widely according to the nature and course of the disease causing death, it is to be expected that a series of brains from a general hospital will show the greatest possible variations in the effects of the fixing fluid. This will apply not only to the encephalon as a whole, but also to the relations of its parts, though perhaps to a less extent. It is consequently wise to use considerable caution in interpreting results based on such material.

To counteract as much as possible the effects of fixation, I have compared the negro brains used by Mall with his white brains—in this way I believe I have as nearly as possible eliminated the effect of changes in the fixing fluid, because the brains of both races were fixed in the same manner and at the same time.

To the brains used by Mall I have added those used by Bean ('06). The two groups do not differ appreciably, so I think no error has been introduced by bringing them together. The larger number is extremely desirable statistically.

The distribution of the percentage weights of these cases is shown in chart 3. The arithmetical average of the percentage weights for the negroes is above that for the whites, and the average for the negro females is above that for the negro males; however, the difference is not a great one and it is not very improbable that a larger number of cases might show the same distribution for the two races. But as far as the results go, they do show a relatively larger cerebellum in negroes. If this indicates anything at all, its significance is probably to be stated in terms of the cerebrum rather than in terms of the cerebellum.

As far as individual cases are concerned, the chart shows clearly that the relative weight of the cerebellum means nothing save in the rarest instances.

THE DISAPPEARANCE OF THE LAYER OF EXTERNAL GRANULE CELLS

Since its discovery by Hess in 1858, the layer of external granule cells has been studied by many investigators. Vignal ('89), in the course of his study of the development of the nervous system, made some observations on these cells and gave us some very good figures showing the histology of the cerebellar cortex at different ages during the fetal period. However, he did not understand the external granule cells; in fact, he thought them pathological, and advanced the theory that they were leucocytes brought to the molecular layer by some inflammation. Since that time there have been several other theories almost as interesting.

At present the external granule cells may be regarded as indifferent cells, some of which become glia cells, while others become nerve cells (Cajal). Of the nerve cells, some migrate to the internal granular layer, while others remain in the molecular layer.

The rate of disappearance of the external layer of cells has been studied in man by Berliner ('05), and by Biach ('09). Their results are shown graphically in chart 4.

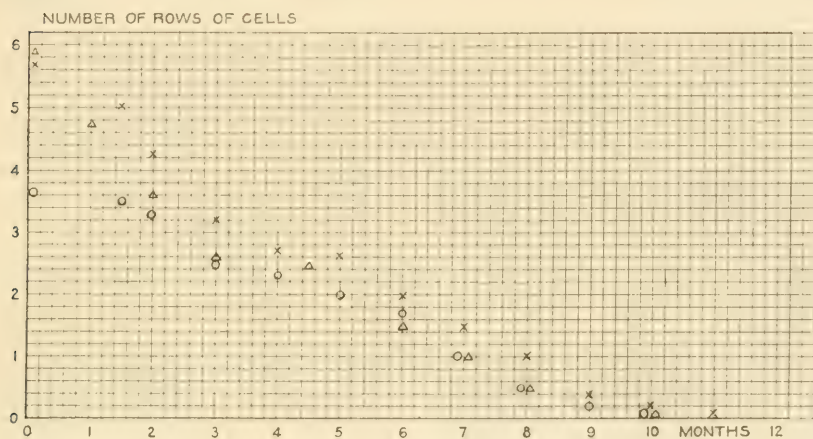


Chart 4 The disappearance of the rows of cells from the external granule layer of man.

Δ	Berliner	} Biach
O	Vermis	
X	Hemispheres	

As will be seen by consulting the chart, Biach finds that at birth there are about six rows of cells in the hemispheres, and that these cells disappear by about the tenth or eleventh month. In the vermis the number is smaller at birth and remains smaller during the period of disappearance, with the result that the layer has usually disappeared by the eighth or ninth month.

Berliner has not made a distinction between the vermis and the hemispheres, so his results are not exactly comparable with those of Biach. They do, however, follow the same course and leave no doubt as to the rate for the cerebellum as a whole.

I have examined twelve cases with ages ranging from eighteen days to eleven months and my results agree so closely with the curve given by Biach that I have not thought it necessary to modify his statement.

Löwy ('10) has studied the external granule layer in a number of birds and mammals. He likewise finds that the vermis is in advance of the hemispheres in the disappearance of the external granule cells. To this he adds the observation that there seems to be a tendency for the cells to disappear faster in the anterior (cephalic) part of the hemispheres than in the posterior. I have studied this in my cases of human cerebella, and although the difference is not a great one, amounting to about one row of cells usually, I consider it to be fairly distinct in the majority of the cases examined. This, theoretically, is what we should expect according to the localization theory of Bolk ('05-'07).

Takasu ('05) has studied the pig and finds there a difference between the vermis and the hemispheres similar to that already noted.

Addison ('11), working on the albino rat, does not find any conspicuous difference between the vermis and the hemispheres, but he does find that the area anterior to the primary sulcus is somewhat in advance of the area posterior to it. Also he finds the paraflocculus to be most retarded of all. As the paraflocculus has been regarded as the center for coördination of tail movements, this appears to me to be a significant observation.

Biach, in connection with his normal cases, also studied the cerebella of twenty-three infants who had died from diseases tending to produce arrest of general development or other abnormalities in the nervous system. Out of the twenty-three cases, ten showed a distinct retardation in the rate of disappearance of the external granule cells; some showed no great variation from the normal, while others were too old to make it certain that they had not been retarded. It is significant, however, that nearly half of his pathological cases do show a correlation between inferior function and retarded disappearance of the external granules. Later I shall consider more specifically the functional significance of the disappearance of this layer of cells.

THE MOLECULAR LAYER AND THE INTERNAL GRANULAR LAYER

We are indebted to Roncoroni ('05) for a careful and extensive series of measurements on the molecular and internal granular layers of the cerebellum in normal and pathological human cases and in a number of lower animals.

He finds that in general the molecular layer decreases in relative thickness and the submolecular layers increase relatively during the course of evolution.

TABLE 9

The thickness in μ of the molecular and submolecular layers in the human cerebellar cortex (Roncoroni). The sex of the idiots is not stated, but probably four out of the five are males

	NUM- BER OF CASES	MOLECULAR LAYER μ			SUBMOLECULAR LAYER μ			MOLECULAR SUBMOLECULAR INDICES			AVERAGE BASED ON FORGOING AVER- AGES
		Minimum	Average	Maximum	Minimum	Average	Maximum	Minimum	Average	Maximum	
Normal men aged about 30 years.	3	250	313	350	150	238	338	100	135	181	131
Idiot, age 20 years.....	1	225	338	363	150	188	250	135	153	193	180
Idiot, age 9 years.....	1	275	313	375	150	188	200	147	178	187	167
Idiot, age 20 years.....	1	250	325	375	113	150	225	144	169	222	213
Idiot, age 25 years.....	1	275	338	425	125	163	250	150	225	340	207
Idiot, age 34 years.....	1	188	250	313	125	163	200	133	150	156	154
Women, aged about 45 years....	3	200	263	313	138	175	225	138	145	150	150
Woman, age 104 years.....	1	188	225	250	138	213	250	83	117	150	106

In table 9 I have condensed those of Roncoroni's results which apply most directly to the present discussion. In his paper he gives the minimum, average, and maximum widths of the molecular and internal granular layers, magnified 80 diameters. He has also given a series of the percentage values obtained by dividing the value for the molecular layer by that for the internal granular layer. From this series I have taken, for the sake of brevity, the minimum, mean, and maximum percentages, and have added in a fourth column the percentage obtained from his average measurements of the two layers.

In table 9 I have reduced these measurements to what they were in μ on the slide. His sections were prepared by the Nissl, Weigert, and Müller-platinum methods, so to get the correct values for the thickness of the layers in the fresh cerebellum it would be necessary to correct his measurements by raising them, probably about 15 per cent, to allow for the shrinkage during dehydration and embedding. However, I have not done this in the table. The relative thickness of the layers is of course not greatly affected by shrinkage.

On consulting his table, several interesting relations become apparent. As shown in the last column of the table, the molecu-

TABLE 10

Thickness of the molecular layer in the lateral lobes of the cerebellum during the first two years (man)

NUMBER	SEX	AGE	THICKNESS IN μ
E22	♂	1 mo. 18 days	175
E13	♂	2 mo. 5 days	193
14250	♂	3 mo. 20 days	200
E23	♂	5?	210
E21	♀	7? mo.	235
E8	♂	10 mo. 6 days	290
14428	♂	12? mo.	320
E18	♂	25 mo. 5 days	330

lar layer is relatively thicker in females than in males, and it is also relatively thicker in idiots than in normal individuals.

I have supplemented Roncoroni's observations by measuring the thickness of the molecular layer during growth. The results are shown in table 10 and in chart 5, and it may be added that the vermis is ahead of the cerebellar hemispheres in the growth of the molecular layer, as well as in other respects already pointed out. Up to the age of about one year the molecular layer is thicker in the vermis, but after that period I find no appreciable difference in the different parts of the cerebellum.

Krohn ('92) finds that in the asymmetric cerebellum of the cat the molecular layer is thicker in the left hemisphere than in

the right. I have studied this relation in eleven human cerebella and have found that in six cases out of the eleven the right molecular layer is absolutely wider than the left, the left is wider in four cases, and the two are the same width in one case. When, however, I divided the values for the molecular layer by those for the internal granular layer so as to get a ratio showing the relative thickness of the two layers, it appeared in ten cases out of the eleven the right molecular layer was relatively thicker than the left, and in the eleventh case the values were identical. It

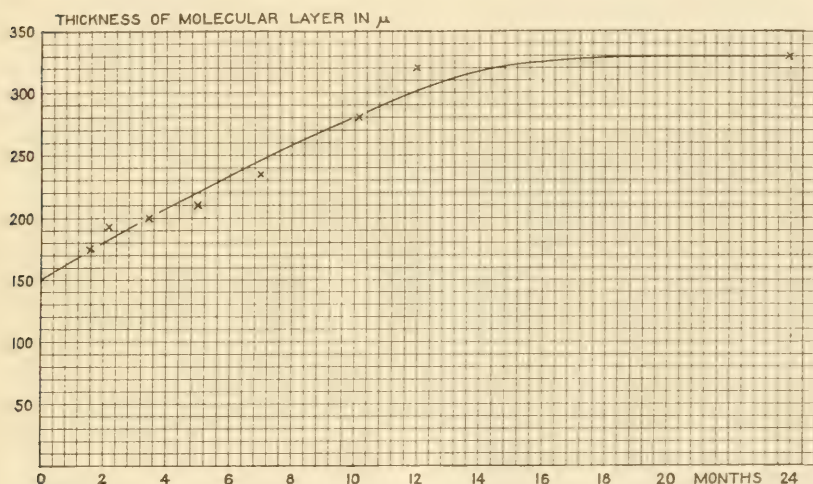


Chart 5 The growth in the thickness of the molecular layer in μ (man) during the first twenty-four months of life.

may be noted also that in only one case was the right internal granular layer absolutely wider than the left. So in man it appears that the right molecular layer is relatively wider then considered in relation to the internal granular layer, and that the left internal granular layer is absolutely thicker than the right. But what functional significance this has is uncertain.

THE PURKINJE CELLS

Growth in size

In the human cerebellum the full number of Purkinje cells is present at birth; they are, however, undeveloped and rather immature in form. The successive stages through which they pass in the growth process have been described in some detail by Cajal and others, but for my purpose it is sufficient to note that by the end of the first year the cells have assumed their adult form.

I have not had satisfactory material for determining the increase in the diameters of the Purkinje cells, but I have made measurements on twelve cases ranging in age from eighteen days to three years. Because of variations in the treatment to which the different brains were subjected, I do not consider the absolute measurements of sufficient value to present them in tabular form. Two results may, however, be stated with a fair degree of assurance. First, the cells are larger in the vermis than in the hemispheres during the first few months of life. Second, the growth in size during the first six months is very rapid, but becomes slower in rate thereafter, and the cells appear to have practically their full size by about twelve to eighteen months. The growth curve has essentially the same form as that shown for the molecular layer in chart 5.

This difference found in the vermis adds to and confirms the other differences already pointed out. There can, I think, be no reasonable doubt that typically the vermis develops in advance of the hemispheres.

The decrease in the number of cells with advancing age

In addition to work already reported, I have made cell counts on the cerebella of sixty-three negroes, whites, and mulattoes of both sexes and of ages ranging from twelve to ninety-two years. All of the material is from The Wistar Institute Museum.

The technique and the method of making cell counts have been the same as that reported in my earlier paper (Ellis, '19). To put the matter briefly, I have made corrections for differences in the size of different cerebella and for the effect of shrinkage of

the tissues during dehydration and embedding, so that I have been able to determine the number of cells in similar fractional parts of each cerebellum. These fractional parts have been called equivalent unit areas and designated by EUA.

In this study I have confined my cell counts to two areas in each hemisphere: first, the area anterior to the primary sulcus, and, second, the area anterior to the great horizontal sulcus, or areas 1 and 3, respectively, as shown in figure 2 of my earlier paper, which is here repeated as figure 1.

Cell counts were made for the four areas, two on the right and two on the left, in each case and the sections were also studied in

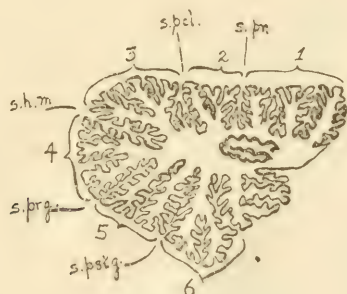


Figure 1

order to estimate the extent to which cells had actually been lost. This is necessary because it is not possible to tell from the number alone whether cells have been lost or are congenitally absent.

After completing the counts I tabulated the results according to age, sex, and color; I have compared the results of the counts for ordinary white males of presumably average intelligence with counts made on white males of superior intelligence; and I have compared also the results for the right and left hemispheres.

As far as my data go, the counts for eleven ordinary white males show no significant difference when compared with the counts for negro males. Neither does any difference appear when the results for the ordinary white males are compared with the results for five white males of superior intelligence. I have

accordingly eliminated these two questions of race and mental grade from my discussion. The three conditions remaining, age, sex, and variations between the right and left sides, will be discussed in turn.

Age. The results of the counts for all the cases were tabulated and plotted according to age. But as cell losses are frequently due to disease, I have eliminated those cases for each age which showed the greatest losses, and have retained as the basis for

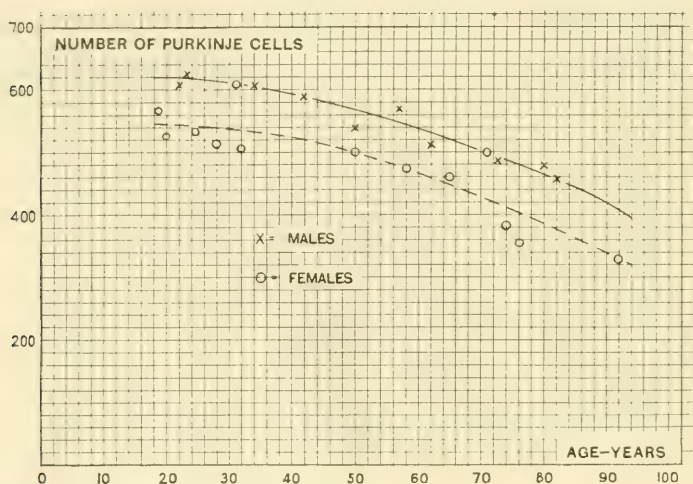


Chart 6 Loss of the Purkinje cells on age (man). X———X, males; O-----O, females. Based on tables 11 and 12.

the chart only those cases which showed the greatest number of cells and the least indiction of cell degeneration for a given age.

By this method I have eliminated forty-three cases, which left a balance of twenty-seven males and thirteen females. To these, for the sake of greater completeness, I have added three cases, all males, reported in my earlier paper. The process of selection described does not materially affect the form of the curve in the chart, although of course it makes it higher. This, however, instead of being a defect, should give us more nearly the true result for the normal biological loss of cells with age. The results are shown in tables 11 and 12, and in chart 6.

TABLE 11

*Number of Purkinje cells per EUA in the cerebella of human males showing the decrease with advancing age. The cases indicated by the * are taken from my earlier paper*

W. I. NUMBER	COLOR	AREAS				TOTAL	AGE
		R-1	L-1	R-3	L-3		
14476	B	171	147	143	144	605	22
14485*	B	165	181	118	160	624	23
15035*	B	169	151	151	138	609	34
14455*	W	169	150	147	125	591	42
Average.....		169	157	140	142	607	22-42
14482	W	161	134	132	112	539	50
14432	W	147	154	142	126	569	57
14464	B	145	127	103	134	509	62
14459	B	127	124	117	123	491	73
14472	B	119	136	118	106	479	80
14483	B	100	124	133	100	457	82
Average.....		133	133	124	117	507	50-82

TABLE 12

Number of Purkinje cells per EUA in the cerebella of female negroes showing the decrease with advancing age

W. I. NUMBER	AREAS				TOTAL	AGE
	R-1	L-1	R-3	L-3		
14477	150	154	137	122	563	19
14475	153	132	107	132	524	20
15047	147	125	127	133	532	25
14466	128	139	119	132	518	28
15057	168	158	130	156	612	31
15039	128	127	122	134	511	32
Average.....	146	139	124	135	543	19-32
14441	128	132	119	120	499	50
15058	108	122	120	122	472	58
15041	144	118	99	99	462	65
15072	143	128	126	108	505	71
15086	90	90	126	96	402	74
15050	107	103	76	103	389	76
15087	87	83	81	83	334	92
Average.....	115	111	107	104	429	50-92

This set of results agrees with and corroborates the results given in my previous paper. There is a gradual loss of cells with advancing age, beginning normally at about the age of thirty to forty years, although this probably varies in different individuals. The anterior (cephalic) part of the cerebellum, as represented by area 1, suffers more than the more posterior part, as represented by area 3. This agrees with the results found by Archambault ('18).

Accompanying the actual loss of cells there are also degenerative changes in those which remain. Chromatolysis, atrophy, vacuolation, and homogeneous degeneration of nucleus and cytoplasm are found. Pigment is likewise present at times (Dolley, '17, '19), but I have not studied it carefully.

Sex. The sex difference shown in chart 6 is one of which I am not at all confident. As far as the results go, they indicate a greater number of Purkinje cells in male cerebella. Men are of course stronger than women, and experimental psychology shows that they are capable of greater motor skill than are women (Thompson, '03); so it is at least possible that there may be a greater number of Purkinje cells in male cerebella. However, a careful study of the sections used convinces me that the difference shown in the chart and tables is due to a greater loss of cells in the female cerebella examined and that it is not a normal difference. But a further study on better material will be necessary to settle the point.

There is no reason, at present, to think of the difference as due to any systematic technical error.

Comparison of right and left hemispheres

Numerous attempts have been made to explain anatomically the greater motor skill which the average person has with his right (or left) hand. Various estimates indicate that probably about 85 or 95 per cent of the population is naturally right-handed, while the remaining 15 or 5 per cent is left-handed. According to Ramaley ('14) right-handedness is a dominant Mendelian unit character, while left-handedness is a recessive unit character.

If this is true, we should expect to find some anatomical basis for the tendency to use one hand rather than the other.

The relation of the cerebellar hemispheres to the body is not entirely clear, but the weight of the evidence indicates that each cerebellar hemisphere controls the muscular coördinations of its own half of the body instead of being crossed, as is the case with the cerebrum. It is consequently interesting to find that when an excessive number of Purkinje cells is lost as a result of advancing age or as a result of disease, the right hemisphere in most

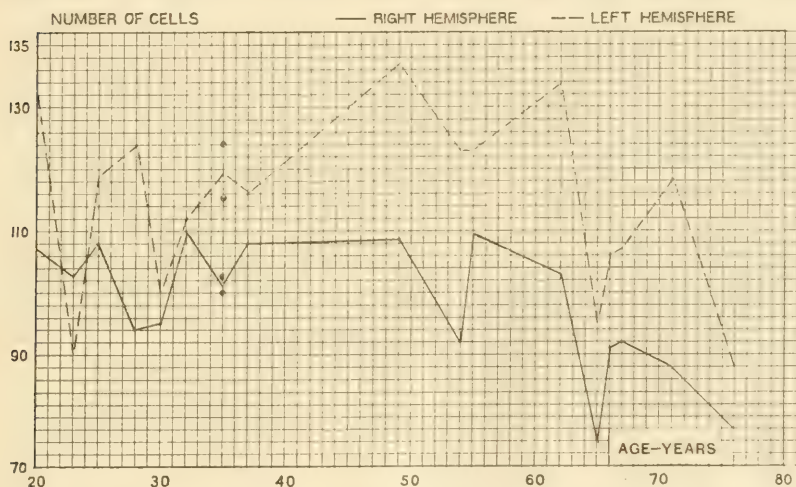


Chart 7 Showing the loss of Purkinje cells on age in the right and left hemispheres of the human cerebellum. —, right hemisphere; -----, left hemisphere.

cases is found to have suffered the greater loss—when compared with what is found in more nearly normal cerebella. To demonstrate this, I have selected from my records the eighteen cases which had suffered the greatest losses of cells, and I have shown in chart 7 the numbers of cells in area 3 of the two hemispheres of this group. Whether the greater loss in the right hemisphere is due to use or to some difference in the vascular system, or to both of these factors, cannot at present be determined. In less extreme cases, as shown in tables 11 and 12, the difference between the hemispheres is not marked in old age.

A further examination of tables 11 and 12 will show that the cases with ages of less than fifty years have in half of the cases a greater number of cells in the right hemisphere. But if we eliminate those cases which show the right hemisphere to be noticeably below normal, the difference becomes more apparent. And, lastly, if we observe the highest values for both hemispheres in the tables we find that in only one case, no. 14485, are the values for the left hemisphere as high as the highest values for the right hemisphere; so that although the problem is a complicated one and the evidence is not entirely conclusive, it seems probable that right-handed people start life with more Purkinje cells in the right hemisphere of the cerebellum.

With this conclusion should be correlated the conclusion stated above to the effect that the right molecular layer considered in relation to the internal granular layer is relatively wider than the left molecular layer. As the molecular layer is the zone in which the dendrites of the Purkinje cells ramify, the relatively greater width of the right molecular layer is a further anatomical characteristic to be correlated with the superior functional efficiency of the right half of the body musculature.

THE GROWTH AND DEGENERATION OF THE MYELIN SHEATHS

Sante de Sanctis ('98) studied the development of the myelin sheaths in the human cerebellum during the first three months of life and found that myelination of the fibers occurs earlier in the vermis than in the hemispheres. I have made no special study of the matter, but it is easy, even in preparations stained with Delafield's hematoxylin, to see that the vermis has the fibers more developed.

Löwy ('10) made a comparative study of the disappearance of the external granule cells and the development of the myelin sheath in lower mammals, and he not only confirms the statement of de Sanctis that the vermis develops in advance of the hemispheres, but he shows that the disappearance of the external granule cells, the development of function, and myelination are closely related. This agrees with the general results of Lui

('94), who correlated the anatomical changes in the cerebellum of man and several lower animals with the development of motor control.

The most detailed statement I have found on the growth of the myelin sheaths in man is from Berliner ('05), and I am quoting it in full:

I have studied more carefully the myelination of the nerve plexus in the granular layer of the vermis. Already in the child of one to two months single myelinated fibers, mostly from the Purkinje cells, can be seen distributed radially; in the fourth month these are more numerous and can be followed to the top of the folium. No myelinated tangential fibers can yet be seen. These appear first at five months; they run below the Purkinje cells and can be seen easier at the bottoms of sulci than at the tips of the folia. In the seventh month the myelinated plexus of the granular layer is well developed; in the ninth month the plexus and the association fibers are still further myelinated; and in the child of fifteen months the association fibers have become still clearer.

From Berliner's statement it will be seen that myelination is taking place while the layer of external granule cells is disappearing and while the child is developing motor control. The growth of myelinated fibers continues for some time, however, at a rather rapid rate after the external granule layer has completely disappeared.

Judging from the results of Engel ('63), there is often a loss or shrinkage of myelinated fibers in the cerebellum during senescence, and this naturally has to be inferred in view of the disappearance of the cell bodies of the Purkinje cells as shown in this paper. To what extent the axones of other cells may disappear or atrophy during senescence I do not know.

THE DENTATE NUCLEUS IN SENESCENCE

Most of the axones from the Purkinje cells in the lateral lobes of the cerebellum terminate in the dentate nucleus, and I have examined therefore the cells of this nucleus to determine what changes take place there during old age. For this purpose I have not attempted to use exact methods, but have simply examined the sections carefully under high and low powers of the microscope.

On the whole, I find that the cells of the dentate nucleus disintegrate and disappear to a much less extent than the Purkinje cells do. In advanced age it is possible to recognize cells in all stages of degeneration and in some cases many cells have been lost. But on the whole, the dentate nucleus appears to suffer less than the cerebellar cortex. With regard to pigmentation, however, the Purkinje cells rarely show the presence of pigment, while many cells of the dentate nucleus show it, and in very old cases few cells are entirely free from pigment.

If we accept the view that this pigment is a product of metabolism and that the failure to eliminate it is an indication of defective function in the nerve cell, we have in the pigmentation of the cells of the dentate nucleus a satisfactory parallel for the actual disintegration of the Purkinje cells. The latter cells rarely show pigment, but, as has been stated, they disintegrate, while the former cells disintegrate to a less extent, but accumulate pigment instead.

THE RELATION OF STRUCTURE AND FUNCTION

In order to correlate some of the growth changes in the cerebellum during the first two years of life, I have prepared chart 8. This shows comparatively the relations of the graphs for the disappearance of the external layer of granule cells, for the increase in the absolute and in the percentage weights of the cerebellum, and for the increase in the thickness of the molecular layer. In each case it will be seen that the period of most rapid growth is completed by the age of twelve months. To this may be added the fact that by that time the Purkinje cells are practically as large as they are in the adult cerebellum. On the functional side, the age of twelve months, or thereabouts, is the time when the child begins to walk. And it is in connection with the increase of functional control that there is an increase in myelinated fibers. The exact relation of myelination and function is, it must be admitted, doubtful; yet there is nothing in the known facts that disagrees with the theory that the myelin sheath is a result rather than a cause of the development of function.

I have pointed out that the vermis is ahead of the lateral lobes of the cerebellum in its early development. This agrees well with the supposition that the vermis is concerned with bilateral movements of the trunk and limbs. The vermis is older phylogenetically than the lateral lobes, and this further suggests that it is the center for the control of the more primitive coordinations of the neuromuscular system.

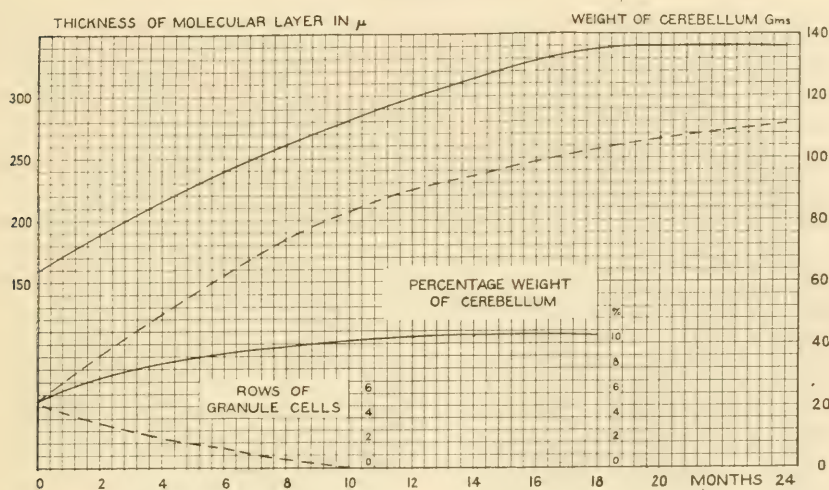


Chart 8 A composite based on charts 1, 4, and 5. The uppermost graph—solid line—gives the changes in the thickness of the molecular layer in μ . Ordinate values at the left. The next below—broken line—gives the weight of the cerebellum in grams. Ordinate values to the right. The next below—solid line—gives the percentage weight of the cerebellum. Ordinate values entered above eighteen months. The lowest graph—broken line—gives the number of rows of cells in the external granule layer. Ordinate values entered above ten months. The grouping of these graphs permits a comparison of several growth changes occurring simultaneously during the first twenty-four months of life.

In that case the earlier development of the vermis agrees well with the fact that the child is able to control many movements of the trunk and limbs before he is able to walk.

In general the head and arm musculature is under control for some months before the child can walk, and this, I think, can be correlated with the earlier disappearance of the external granule cells in the anterior part of the cerebellum.

As far, then, as the growth changes have been studied, they are found to be closely correlated with the development of function.

It is hardly necessary to add here to what has already been said about the correlation between the disappearance of the Purkinje cells in old age and the impairment of motor strength and skill. The two go hand in hand.

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Estudios comparados sobre el crecimiento del cuerpo calloso.

I. Sobre el área del cuerpo calloso, medida en secciones sagitales
del cerebro de la rata albina.

Empleando cortes sagitales del cuerpo calloso de setenta y seis ratas albinas, el autor ha obtenido los siguientes resultados: En la rata albina el cuerpo calloso del recién nacido no contiene fibras mielínicas. Estas aparecen desde el séptimo hasta el décimo día. Desde el nacimiento hasta la edad adulta el área del cuerpo calloso aumenta unas 3.5 veces. Este aumento tiene lugar en tres fases: Una fase temprana, que comprende los diez primeros días de la vida, durante la cual aparecen nuevos axones sin mielina, aumentando de diámetro los formados previamente; una segunda fase desde el décimo hasta el trigésimo día, durante la cual la formación de nuevas vainas de mielina es el factor principal, y una tercera fase después del trigésimo día, en la cual el cambio mas principal es el aumento de diámetro de las fibras mielínicas. Cuando se mide el grosor del cuerpo calloso durante el crecimiento al nivel de la rodilla (genu), tronco y rodete (splenium) se observa que el crecimiento proporcional es mayor en la primera y menor en el último. Una comparación del desarrollo del cuerpo calloso en el hombre y rata adultos demuestra que el área relativa del cuerpo calloso en el hombre es distintamente mas grande que en la rata (en el hombre es de 4.44 por ciento y en la rata de 3.29 p.c.). El crecimiento del cuerpo calloso medido por el número de fibras mielínicas y el área de las secciones transversales está relacionado con el desarrollo psíquico del animal.

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COMPARATIVE STUDIES ON THE GROWTH OF THE CORPUS CALLOSUM

I. ON THE AREA OF THE CORPUS CALLOSUM, MEASURED ON THE SAGITTAL SECTION OF THE ALBINO RAT BRAIN

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TWO FIGURES AND FOUR CHARTS

Concerning the exact function of the corpus callosum there is still much question. The importance of the callosum in man is, however, clear from the fact that its absence or disease of it is often attended by more or less profound weak-mindedness or downright idiocy (Eichler, Knox, Urgart, Ward, Huppert, Gausser: cited from Onufrowicz, '87; Kaufmann, '87; Hochhaus, '93).

Some cases of the partial absence of this structure do not exhibit, however, any serious deviation from the normal, though such individuals have been classed by their acquaintances as 'queer' (Nobiling-Bayer, Birch-Hirschfeld, Jolly: cited from Onufrowicz, '87).

Spitzka ('07) and Cameron ('17) have stated that the area of this commissure in the sagittal section is unusually large in the brains of individuals of recognized intellectual ability.

Further, Spitzka ('07) stated that the size of the callosum bears a relationship to the degree of intellectual superiority. Whether or not Spitzka is right in declaring that talented men have larger callosa when compared with ordinary men, can be answered only after a more complete study on the growth of callosal area in man, when considered in relation to the recorded brain weight and the abundance of the convolutions.

As a first step toward further knowledge of this structure, I have undertaken, at the suggestion of Professor Donaldson, to

determine the growth between birth and maturity of the area of the callosum measured on the median sagittal section of the albino rat brain. The object in undertaking such a study was to throw some light upon the following questions:

1. In what manner does the white substance of the mammalian brain increase after birth?

2. What is the relation in the rat between the increase in the area of the callosum, the myelination of the fibers in it, and the psychical development of the animal?

3. How does the growth of the area of the callosum in the rat compare with the corresponding growth change in man?

For the psychical development of the rat the studies made by Watson ('03) and Lane ('17) have been mainly consulted. On looking into the literature, nevertheless, I found many references concerning the presence of mental associations in rodents, as indicated by the formation of habits, though Flechsig ('96) denies the presence of association centers as defined by him. Although the callosal fibers form only one system of commissural fibers in the brain, yet they constitute such a large fraction of this group that changes in them must be of the greatest importance for the psychical life of the rat.

In connection with this study I desire to express my sincere thanks to Doctor Greenman, Director of The Wistar Institute, for putting the facilities of the laboratory at my disposal, and also to acknowledge my obligations to Professor Donaldson, under whose direction this research has been made.

MATERIAL AND TECHNIQUE

a. Fixation

For the measurement of the callosum it is desirable to have material which has suffered the least possible change in volume as the result of fixation and also to employ a uniform technique. When the rat brain is fixed in formalin for sixteen hours followed by Weigert's rapid mordanting fluid for five days, the shape and weight of the total brain suffer but little as the result of the treatment.

b. The method of procedure

The material was obtained from seventy-six albino rats (fifty males, twenty-six females), all from the rat colony at The Wistar Institute. Each rat was chloroformed and notes made on the age, sex, body weight, and body length. After dissection the entire brain was severed from the spinal cord at the level of the calamus scriptorius and weighed to a milligram in a closed weighing bottle. The brain was next transferred to a 10 per cent formalin solution for from twelve to sixteen hours at room temperature, the basal surface of the brain being in contact with the bottom of the vessel. Then sagittal slices, which contain the entire callosum—about 3 mm. in thickness and including the plane from which the section was to be taken—were placed in Weigert's rapid mordanting fluid for from four to five days. After being washed with running water and passed through the alcohols, they were put in ether-alcohol for a day and then imbedded in parlodion. A short series of sagittal sections 20μ thick was cut so as to include one in the median plane, which was used for study. These were treated by the Kultschitzky-Wolter's myelin stain method, modified slightly to obtain the best results from this particular tissue. In detail the modified method is as follows:

After cutting in 70 per cent alcohol, the sections were passed to distilled water, then mordanted in Kultschitzky's fluid for twelve hours at a temperature of 37°C . They are then well washed with tap-water, and brought into a decolorizing solution composed of

	<i>parts</i>
Borax.....	2.0
Ferrieyanide of potassium.....	2.5
Aqua distillata.....	200.0

They were kept in this solution from ten to twenty minutes, or until complete differentiation of the fibers, and then were well washed with running water, dehydrated, cleared with creosote, and mounted in neutral canada balsam.

MEASUREMENT AND ENUMERATION

Great care was taken to select the section nearest the median plane. The selected sections from the several brains were projected on a sheet of paper with a Leitz-Edinger projection

TABLE 1

Showing the age, sex, body length, body and brain weights, and area of callosum of the seventy-six normal albino rats used in this study, entered by litters according to increasing age

LITTER	SEX		AGE	BODY WEIGHT	BODY LENGTH	BRAIN WEIGHT	AREA OF CORPUS CALLOSUM
	Male	Female					
			<i>days</i>	<i>grams</i>	<i>mm.</i>	<i>grams</i>	<i>mm.²</i>
1	2	1	Birth	4.3	43	0.242	1.45
2	2	1	5	6.5	53	0.408	2.07
3	2	2	7	9.5	61	0.726	2.34
4	2	1	10	7.6	58	0.692	2.38
5	2	1	12	27.4	101	1.372	3.25
6	2	1	15	15.7	79	1.115	2.39
7	2	1	17	21.5	88	1.256	2.42
8	2	1	20	31.5	104	1.407	2.86
9	2	1	22	29.9	104	1.266	2.84
10	2	1	25	26.2	103	1.364	3.17
11	2	1	27	27.4	101	1.372	3.58
12	1	2	30	29.2	106	1.378	3.68
13	2	1	35	27.5	101	1.404	3.35
14	1	1	40	59.2	134	1.585	4.28
15	2	1	50	75.3	147	1.572	4.43
16	3	1	60	76.5	143	1.502	4.35
17		3	70	75.1	145	1.454	3.99
18	2		80	100.6	159	1.645	4.52
19	2	1	90	101.3	156	1.588	4.51
20	3	1	100	103.5	164	1.657	4.50
21	4		112	133.2	167	1.700	4.60
22		2	122	134.3	174	1.700	4.61
23	3	1	150	159.7	179	1.701	4.67
24	2		205	220.8	197	1.713	5.28
25	1	2	378	274.8	218	1.716	5.29

apparatus, at a magnification of exactly twenty diameters, and the outline accurately traced. At the transition of the splenium corporis callosi to the psalterium, the boundary line was drawn along the largest fibers of the fornix longus. The area of the callosum in the drawing was then measured three times to a

square millimeter, using the Amsler planimeter. The values obtained were averaged, reduced to the actual values for the area of the corpus callosum on the slide, and recorded. As I measured all the sections in the same manner, the data thus obtained are comparable among themselves. These data are presented in table 1 in a condensed form, but the individual records have been filed in the Archives of The Wistar Institute.

GROWTH IN AREA OF THE CALLOSUM IN SAGITTAL SECTION

a. Growth in callosal area on body weight

Table 2 is based on table 1 and contains the records for the area of the brain as well as the callosum.

According to Donaldson ('08), the brain weight goes with the body weight in so nearly a like manner in both sexes that we have felt justified in combining our observations on males and females both in the tables and for discussion.

Chart 1 shows how the observations given in table 2 are distributed when entered in relation to increasing body weight, which in turn implies increasing brain weight. As can be seen by inspection (column D, table 2), the 'scatter' of the entries is not very great. It is of interest to find that the mean observed values (dotted line in chart 1, A) follow closely the theoretical logarithmic curve. The theoretical curve, about which the observations cluster, is represented by the continuous line in chart 1, A, and was computed by means of the formula:

$$y = 0.184 + 0.0003 x + 2.08 \log x \dots \text{Formula (1)}$$

in which y is the area of the callosum in the sagittal section, in millimeters, and x the weight of the body, in grams. This formula is based on the general formula $y = a + bx + c \log x$, already published by Hatai ('11). The values of x and y are given in column A and E of table 2. The theoretical curve based on this formula gives a very good graduation of the area of the callosum for any value of x . An examination of chart 1, A, shows that the growth curve of the callosal area can be divided into two parts: 1) the period of earlier and more rapid

growth, represented by a curve, and, 2) the period of later slow growth, represented by the straight line.

The body weight of about 125 grams (75 days) corresponds to the transition point of the two periods. Figure 1 gives a

TABLE 2

Giving the mean observed and calculated area of the brain and of the corpus callosum on observed body weight in the albino rat. In columns G to H the relations of the callosal area to the total brain area are given

LITTER NUMBER	NUMBER OF CASES	BODY WEIGHT— OBSERVED	TOTAL BRAIN WEIGHT— CALCU- LATED	AREA OF ENTIRE BRAIN— CALCU- LATED	AREA OF CORPUS CALLOSUM		C×0.0344	F - E	$\frac{E}{C}$
		A	B	C	Ob- served	Calcu- lated			
					D	E	F	G	H
		grams	grams	mm. ²	mm. ²	mm. ²	mm. ²	mm. ²	per cent
1	3	4.3	0.200	34.2	1.45	1.51	1.18	-0.33	4.4
2	3	6.5	0.401	54.4	2.07	1.88	1.87	-0.01	3.5
3	4	7.6	0.506	63.5	2.38	2.02	2.18	0.16	3.2
4	3	9.5	0.654	75.4	2.34	2.22	2.59	0.37	2.9
5	3	15.7	1.035	102.2	2.39	2.69	3.51	0.82	2.6
6	3	21.5	1.186	112.0	2.42	2.96	3.85	0.90	2.6
7	3	26.2	1.260	116.6	3.17	3.15	4.02	0.88	2.7
8	3	27.4	1.277	117.7	3.25	3.18	4.09	0.91	2.7
9	3	27.4	1.277	117.7	3.58	3.18	4.09	0.91	2.7
10	3	27.5	1.279	117.9	3.35	3.18	4.06	0.88	2.7
11	3	29.2	1.299	119.1	3.68	3.25	4.09	0.84	2.7
12	2	29.9	1.311	119.9	2.84	3.27	4.13	0.86	2.7
13	3	31.5	1.318	120.3	2.86	3.31	4.14	0.83	2.8
14	2	59.2	1.521	132.2	4.23	3.88	4.54	0.66	2.9
15	3	75.1	1.590	136.2	3.99	4.11	4.68	0.57	3.0
16	4	75.3	1.591	136.4	4.43	4.12	4.69	0.58	3.0
17	3	76.5	1.595	136.6	4.35	4.13	4.71	0.59	3.0
18	2	100.6	1.669	140.7	4.51	4.38	4.84	0.46	3.1
19	3	101.3	1.675	141.1	4.50	4.39	4.85	0.46	3.1
20	4	103.5	1.681	141.5	4.51	4.40	4.88	0.49	3.1
21	3	133.2	1.746	145.0	4.60	4.63	4.99	0.35	3.2
22	2	134.3	1.749	145.2	4.61	4.66	4.99	0.34	3.2
23	4	159.7	1.794	147.5	4.67	4.81	5.09	0.28	3.3
24	2	220.8	1.880	152.3	5.28	5.12	5.23	0.11	3.4
25	3	274.8	1.937	155.4	5.29	5.34	5.34	0.00	3.4

series of outlines of the callosum at six ages, showing the increase in area and the change in shape. At seventy-five days the outline of the callosum is a little smaller than that shown at E.

It is important to consider the factors responsible for producing the differences between the rapid and the slow growth of the callosal area during these two periods. We should have information touching the changes in, 1) histological structure; 2) the degree of myelination; 3) the chemical composition; 4) the change in the percentage of water and any other modifications occurring during growth, which can be applied.

1. The callosum is pure white matter, except for a small amount of glia cells, the longitudinal striae and blood-capillaries,

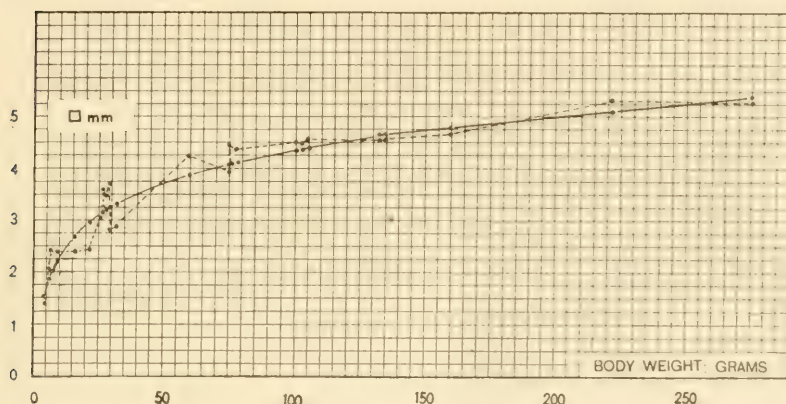


Chart 1A The continuous line represents the area of the corpus callosum according to body weight, calculated by formula 1; the broken line shows the means of the observed callosal areas. Albino rat.

and the callosal fibers are without a neurilemma. Koch ('17) found in the dog and in man a great similarity of chemical composition represented by the weight of the ether-alcohol extract from the callosum and the intradural nerve roots. From these results Donaldson ('17) concluded that the degree of myelination was probably similar in these two parts of the nervous system. We know also from Sugita's work that during cortical growth, both the axon and its myelin sheath lengthen and enlarge without disturbing their relative volume relations, and that the very considerable increase in the area of the cortex,

after its thickness is attained, is largely caused by the thickening of the fibers and the formation of the myelin sheaths (Sugita, '17).

According to the measurements of Donaldson and Nagasaka ('18), which were made on the largest fibers in the dorsal and ventral roots of a spinal nerve, all such fibers enlarge to the same extent, and the axis-sheath relation in the fibers was found

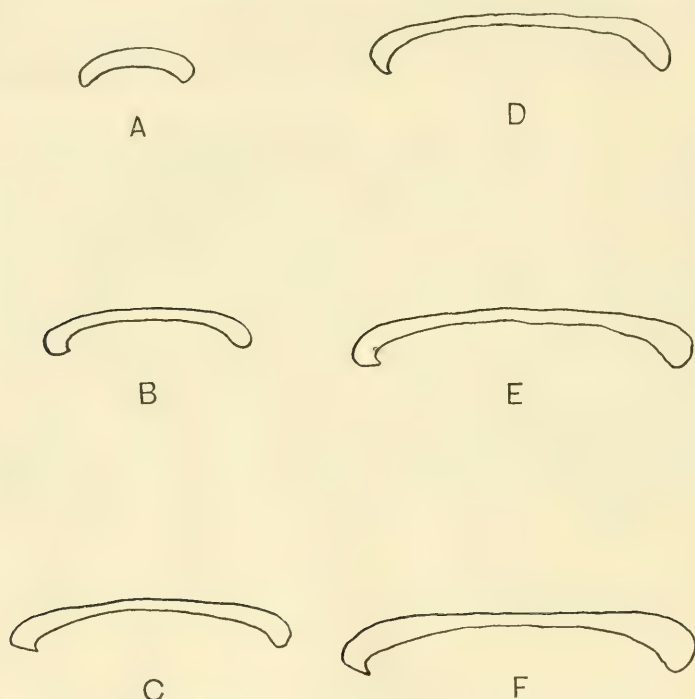


Fig. 1 Outline drawings of the cross-section of the corpus callosum. Albino-rat. Enlarged ten times. A, Just born; B, 10th day; C, 20th day; D, 30th day; E, 100th day; F, 378th day.

to be such that the area of the axis in the youngest groups was about 40 per cent of the area of the section of the entire fiber, but this increases with the advancing age of the rat until it becomes about 50 per cent in the old animals. Certainly, my preparations suggest that after the rather rapid increase in the area, the number of fibers is not much increased during later growth.

2. Concerning myelination in the callosum, we have noted the following: A small number of scattered myelinated fibers is found at the tenth day after birth. This number increases gradually till the twenty-fifth to twenty-seventh day, at which age the myelinated fibers are evenly distributed over the entire section.

After this period the myelinated callosal fibers grow mainly in size rather than in number up to at least the 378th day. Thus the great increase of the callosal area, which takes place after the tenth day, appears to be due for the most part to the increase in the diameter of the fibers combined with the formation of new myelin sheaths.

3. As shown by Koch ('17, table 3), the callosum exhibits the chemical changes characteristic for white matter, and thus during growth it shows a rapid and large increase in lipoids and a corresponding decrease in its water content.

4. According to Koch ('17), the corpus callosum of the human brain loses from 18 per cent to 20 per cent of water, while, owing to the slight admixture of myelinated fibers, the gray matter loses only from 2 to 5 per cent of water from birth to maturity. These changes in the water content, which are associated with the change in the lipoid content, are much greater, therefore, in the corpus callosum than in the cortex, in which the changes are only slight.

b. Comparison between the growth of the callosal area and of the total brain area

From the brain weights on the observed body weight (calculated from the formula $\text{Br. W.} = 0.554 + 0.569 \log (\text{body weight} - 8.7)$ as are given in column B and C, table 2, we can express the area of the total brain, considered as a cube, by the values for the square of the cube root of the brain weight. In this treatment the variations in the specific gravity of the brain have been neglected. In chart 1, B, the upper curve represents the area (reduced) of the total brain, on body weight, the actual values of the ordinates being reduced by multiplying by the

factor 0.0344, which makes identical both the brain area and the callosal area at the body weight of 274.8 grams. Column F of table 2 shows the reduced values. The difference between the reduced values of the total brain and the callosal area are represented in column G (F-E). These differences increase rapidly from a body weight of 7.6 grams as the age advances and they reach the maximum (F-E = 0.91) at a body weight of 27.4 grams, then decrease slowly, at last reaching 0 point at the body

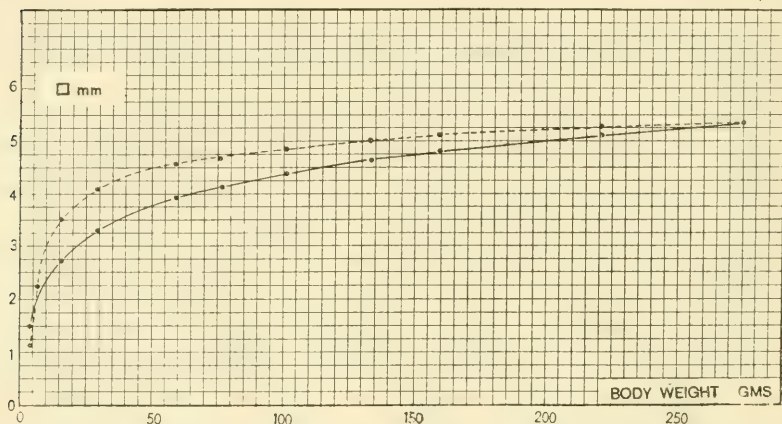


Chart 1B In the upper curve the broken line shows the total brain area according to body weight as calculated by the formula $(\sqrt[3]{\text{brain weight}})^2 \times 0.0344$ in order to make these two curves comparable at the last entry. In the lower curve, the continuous line shows the area of the corpus callosum according to body weight as calculated by formula 1. Albino rat.

weight of 274.8 grams. The course of the ordinate differences may be divided into three phases:

Phase 1 (from sixth to tenth day). This represents small differences from 0.16 to 0.37 mm.^{2*}

Phase 2 (from twelfth to thirty-fifth day). The maximum difference is 0.91 mm.², the initial 0.82, and the final 0.83 mm.²

* From birth to six days the reduced brain area is smaller than the callosal area. This anomalous result is chiefly due to the fact that the calculated rather than the observed brain weights were used. I take this discrepancy to be the result of computation.

Phase 3 (from thirty-sixth to 378th day). The initial difference is 0.66 mm.², and from this point on the difference value decreases very slowly till it becomes zero.

To explain the slower growth of the callosal area compared with that of the entire brain, it will be necessary again to touch on, 1) the change in histological structure; 2) the development of myelin; 3) the later growth of the myelinated fibers as a whole.

1. Since the entire brain is composed of both white and gray matter, while the callosum represents white matter only, the growth of the total brain depends on the growth of both the cell bodies and the fibers, while that of the callosum depends on the growth of fibers alone. According to Sugita's ('18) studies on the development of the cerebral cortex in the rat, the thickness of the cortex, the total number of the nerve cells in it and the size of these cells have all attained nearly their full values at about the age of twenty days. The further development after this age is represented principally by growth of the fibers and their myelin sheaths. The growth of the callosal area during the first twenty days after birth is more rapid than the process of myelination in it.

There must therefore be a steady addition of the new unmyelinated fibers. Although the general form of the growth curve of the callosal area is similar to that of the total brain area, nevertheless the rate of the former is slower for about twenty to thirty days after birth, a period at which the nerve cells grow very rapidly, as the observations of Sugita show. Thus we conclude that the difference here noted between these two curves is due in a large measure to the presence of the cell bodies in the brain and their absence from the corpus callosum.

2. So far as the appearance of the myelinated fibers in the callosum is concerned, these fibers myelinate from about the tenth day on rather slowly, but at about twenty days of age, the myelination process becomes more rapid, and at the thirtieth to the thirty-fifth day the myelinated fibers in the callosum are present in large numbers.

During and after this phase the cortical area increases chiefly by the deposition of the myelin sheaths. The fact that the

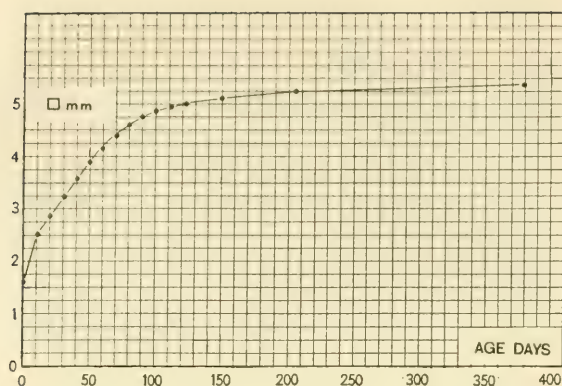


Chart 2 The growth curve of the callosal area according to age. Albino rat.

TABLE 3

Showing the calculated callosal area at different ages of the albino rat. Data on standard body weight are taken from table 74, 'The Rat' (Donaldson, '15), and the calculated callosal area determined by formula 1

NUMBER	AGE	BODY WEIGHT		AREA OF CORPUS CALLOSUM		BRAIN WEIGHT—STANDARD
		Observed	Standard	Observed	Calculated from C.	
	A	B	C	D	E	F
	days	grams	grams	mm. ²	mm. ²	grams
1	Birth	4.3	4.7	1.45	1.58	0.217
2	5	6.5	7.6	2.07	2.02	0.509
3	7	9.5	9.5	2.34	2.22	0.657
4	10	7.6	13.5	2.38	2.54	0.947
5	12	27.4	14.4	3.25	2.60	0.991
6	15	15.7	16.1	2.39	2.71	1.057
7	17	21.5	17.3	2.42	2.77	1.095
8	20	31.5	19.5	2.86	2.87	1.150
9	22	29.9	21.1	2.84	2.94	1.184
10	25	26.2	23.9	3.17	3.06	1.237
11	27	27.4	25.9	3.58	3.13	1.266
12	30	29.2	29.2	3.68	3.25	1.311
13	35	27.5	35.4	3.35	3.42	1.375
14	40	59.2	42.5	4.23	3.59	1.434
15	50	75.3	59.6	4.43	3.90	1.537
16	60	76.5	80.3	4.35	4.15	1.622
17	70	75.1	104.7	3.99	4.42	1.695
18	80	103.5	132.8	4.51	4.63	1.758
19	90	100.6	150.5	4.51	4.76	1.791
20	100	101.3	165.8	4.51	4.85	1.817
21	112	133.2	181.6	4.60	4.94	1.841
22	122	134.3	193.1	4.61	5.01	1.857
23	150	159.7	218.7	4.67	5.12	1.888
24	205	220.8	250.9	5.28	5.25	1.924
25	378	274.8	279.9	5.29	5.36	1.954

cortex attains nearly its full thickness before the callosal fibers are myelinated would contribute to the great difference in these two curves at twenty to twenty-five days after birth.

The cerebral cortex also has numerous radiating fibers, the myelination period of which is nearly identical with those fibers in the callosum (Watson, '03).

In general, the growth of the callosal area has a tendency to be longer continued than that of the total brain area, as is quite evident from these two curves. This is in agreement with the results found by Donaldson and Nagasaka ('18) in the fibers of a spinal nerve.

3. On looking at the data in table 74, 'The Rat' (Donaldson, '15), we see that between birth and 365 days the decrease in the percentage of water in the spinal cord is greater than that in the brain; the spinal cord loses 17.6 per cent of water, while the brain loses 10.5 per cent.

This difference is due chiefly to the fact that the spinal cord contains a greater proportion of myelinated fibers. The callosum ought therefore to show a greater similarity to the spinal cord than to the brain in this respect, and this conclusion is supported by the observation of Koch (17); the human callosum loses from 18 to 20 per cent of water.

c. Growth of the callosal area on age

To determine the growth of the callosal area on age in the albino rat, the calculation according to the previous formula was made for each callosal area, using age groups, and the results are given in column E, table 3, and plotted in chart 2. The data on the standard body weight in column C were taken from table 74, 'The Rat' (Donaldson, '15). The growth curve of the callosal area on age is very much the same as that plotted on body weight, except that the rapid rise appears early.

On examining chart 2 we notice three phases corresponding to the two phases in chart 1 in which the callosal areas are arranged according to the corresponding body weight; that is, a first phase of rapid increase which covers the first ten days after birth, a

second phase of slower increase which extends through the period of sexual maturity (about seventy to eighty days), and the third phase of slow increase which extends from eighty days on.

It is clear that the callosal area increases most rapidly before myelination by the growth and addition of new fibers during the first ten days after birth. From ten days up to sexual maturity, the area increases not only by the addition and enlargement of the fibers, but largely by the formation of the myelin sheaths. After sexual maturity is reached, the callosal area

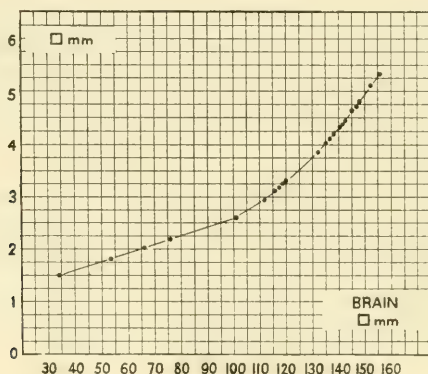


Chart 3 The base line represents the total brain areas from 30 to 155 sq.mm. The corresponding values for the callosal area are measured on the ordinates as shown by a theoretical curve based on formula 1. Albino rat.

still continues to increase up to 378 days, chiefly by the enlargement of the fibers already myelinated.

d. Growth of the area of the callosum on the total brain area

The calculated values for the callosal and total brain areas on the observed body weight are given in columns C and E, table 2. When the callosal areas are plotted on the total brain areas, the relations of the data are shown in chart 3, in which we may recognize the following three phases in the relative growth of the callosal area.

1. From birth to fourteen days the callosal area increases relatively slowly. To brain weight = 1 gram; brain area, 102 mm.²

2. Between fourteen days and seventy-five days the callosal area increases relatively very rapidly. To brain weight = 1.74 grams; brain area, 145 mm.²

3. From the seventy-fifth to 378th day the increase is a little more rapid than in the second phase.

These are approximately the same relations as shown in chart 1, B, but presented in a different form. The explanation of the relations is that which was given earlier.

e. Comparison of the growth ratio between the callosal area, the total brain area, and the cortical area (in sagittal section) on brain weight

For this study we utilized the corrected values of the cortical area in sagittal sections from table 1 of Sugita ('18), deriving the values for our series of brain weights from Sugita's data, and these are given in column H, table 4. The data on the brain weights copied from column B, table 2, are given in column C, table 4. If the initial values of the three areas are taken respectively as unity, we obtain ratios for the succeeding values as given in columns E, G, I, table 4.

These data are presented in chart 4, on the brain weight. From this we see that the ratio of the callosal area increases regularly but slowly up to a brain weight of about 1 gram—equivalent to about twelve days—after which the increase is more rapid. A study of the chart shows that in the case of both the entire brain and the cortex the increase in the ratio is more rapid than in the case of the callosum during the first twenty to twenty-five days (= brain weight of 1.20 grams), while after that it is slower.

Generally speaking, the growth rates of these areas just mentioned show a rapid increase during the first twelve days, and after this period the growth rate becomes slower and the three curves take a somewhat parallel course.

According to the opinion of Watson and other authors, the psychical life of the rat reaches a high degree of development by the twenty-seventh day, and I have also noted that at this time the myelinated fibers are evenly distributed throughout the

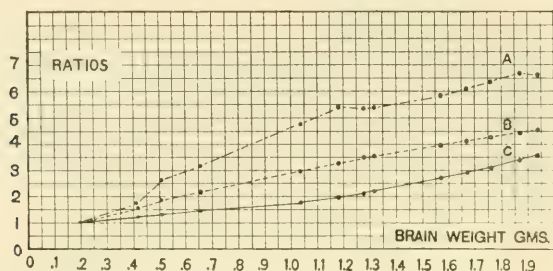


Chart 4 Showing the ratios of the values for the callosal area, total brain area, and cortical area (sagittal section) of the albino rat, according to the brain weight. *C*, the ratios of the computed callosal area; *B*, the ratios of the computed total brain area; *A*, the ratios of the computed cortical area in sagittal section. Albino rat.

TABLE 4

Giving from birth to maturity the ratios of the callosal area, of the total brain area, and of the cortical area in sagittal section on brain weight. All values are calculated according to each brain weight group. Albino rat

NUMBER	NUMBER OF CASES	BRAIN WEIGHT—CALCULATED	AREA OF CORPUS CALLOSUM—CALCULATED	RATIO	AREA OF TOTAL BRAIN—CALCULATED	RATIO	AREA OF CORTEX SAGITTAL SECTION—FROM SUGITA'S TABLE	RATIO
A	B	C	D	E	F	G	H	I
		grams	mm. ²		mm. ²		mm. ²	
1	3	0.200	1.51	1.0	34.2	1.0	4.6	1.0
2	3	0.401	1.88	1.2	54.4	1.6	9.4	2.0
3	4	0.506	2.02	1.3	63.5	1.9	11.8	2.5
4	3	0.654	2.22	1.5	75.4	2.2	15.9	3.4
5	3	1.035	2.69	1.8	102.2	3.0	23.3	5.0
6	3	1.186	2.96	2.0	112.0	3.3	27.0	5.8
7	15	1.278	3.19	2.1	117.8	3.4	26.7	5.8
8	6	1.314	3.29	2.2	120.1	3.5	27.1	5.9
9	12	1.574	4.06	2.7	135.4	4.0	29.0	6.3
10	9	1.675	4.39	2.9	141.1	4.1	29.5	6.4
11	10	1.763	4.70	3.1	145.9	4.3	31.7	6.9
12	2	1.880	5.12	3.4	152.3	4.4	33.5	7.3
13	3	1.937	5.34	3.5	155.4	4.5	32.5	7.0

entire callosum; that is, the callosum at this age is approximately mature in respect of the number of myelinated fibers in it. The relations shown by the ratios in chart 4 are in harmony with these events.

f. Thickness of the corpus callosum

As to the first appearance of the callosum, Hamilton ('86) and Goldstein ('03) both state that in man it appears in the end of the third or the fourth month of intra-uterine life.

In the rat, according to Zuckerkandl ('09), the callosum appears in the fetus of 19 mm., which, according to Stotsenburg ('15), corresponds to about the eighteenth day of fetal life.

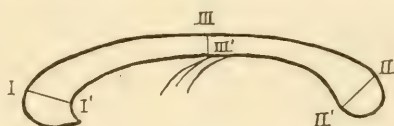


Fig. 2 Outline of the callosum. Showing at what localities the measurements listed in table 5 were taken.

To follow the growth of the callosum I have measured its thickness in three localities I-I', II-II', III-III'. Figure 2 shows the position of the localities at which the thickness of the callosum was carefully determined. These localities have been selected as fairly representative of the entire callosum.

Locality I. The maximum diameter of genu on the line of I-I'.

Locality II. The line II-II' represents the maximum thickness of splenium.

Locality III. This gives the maximum thickness of truncus, which is represented by the line III-III' drawn at the point just before the fornix longus fibers make contact with the callosum.

The measurements for thickness have been made under the microscope with a low-power lens, but for the measurement of the callosal length I have used a sliding calipers reading to a tenth of a millimeter, the entire callosum being too large to

measure under the microscope (table 5). For the purpose of discussion the data in table 5 have been condensed as in table 6. In this series (table 6) the genu has the greatest thickness and

TABLE 5

Showing the average thickness at the genu, splenium, and truncus in sagittal sections of the rat's callosum according to age

LITTER NUMBER	NUMBER OF CASES	AGE	LENGTH	THICKNESS OF CORPUS CALLOSUM		
				Genu	Splenium	Truncus
A	B	C	D	E	F	G
		<i>days</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>
1	3	Birth	2.22	0.32	0.35	0.29
2	3	5	3.10	0.35	0.36	0.18
3	4	7	3.55	0.34	0.37	0.24
4	3	10	3.82	0.29	0.37	0.17
5	3	12	5.50	0.37	0.35	0.19
6	3	15	4.38	0.34	0.34	0.15
7	3	17	4.54	0.34	0.22	0.18
8	3	20	5.35	0.36	0.35	0.20
9	3	22	5.37	0.36	0.28	0.19
10	3	25	5.48	0.36	0.37	0.18
11	3	27	5.52	0.41	0.38	0.22
12	3	30	5.50	0.36	0.39	0.23
13	3	35	5.17	0.40	0.37	0.20
14	2	40	5.87	0.44	0.39	0.30
15	3	50	6.19	0.45	0.44	0.28
16	4	60	6.02	0.37	0.36	0.25
17	3	70	6.05	0.45	0.33	0.35
18	2	80	6.10	0.49	0.42	0.27
19	3	90	6.37	0.48	0.36	0.24
20	4	100	6.32	0.48	0.39	0.25
21	4	150	6.22	0.53	0.42	0.33
22	2	205	6.92	0.59	0.47	0.29
23	3	378	6.66	0.58	0.35	0.28

the truncus the least, but when the values in the first age group are compared with those in the last, it is seen that the ratio of increase is genu 1.56, truncus 1.40, and splenium 1.21. Thus the growth in thickness has been greatest at the frontal end of the callosum and least at the occipital end.

It is of interest to note that at birth the callosal area is relatively large compared with the area of total brain (table 2) and furthermore that the thicknesses of the three parts (genu, splenium, and truncus) are more similar at birth than they are at later ages. Table 5 shows these latter relations.

DISCUSSION

I wish now to present some answers to the questions raised at the beginning of this paper.

1. If the callosum is taken as typical for the white matter of the brain, then we may state the manner of its increase in the following general terms:

TABLE 6

Showing the average values for the length and the thickness of parts of the callosum arranged in three age groups. Based on table 5

AGE GROUP	LENGTH	GENU	RATIO	SPL- NIUM	RATIO	TRUNCUS	RATIO
	<i>mm.</i>	<i>mm.</i>		<i>mm.</i>		<i>mm.</i>	
Birth to 22 days.....	4.20	0.34	1.0	0.33	1.0	0.20	1.0
25 to 80 days.....	5.77	0.41	1.20	0.38	1.15	0.25	1.25
90 to 378 days.....	6.50	0.53	1.56	0.40	1.21	0.28	1.40

The first phase of growth is characterized by the addition of new axones and the growth in diameter of the axones already present in the callosum, but it is not till the end of this phase that the myelin sheaths appear.

In the second phase the addition of new fibers becomes relatively less important—the greatest change is caused by the rapid formation of the myelin sheaths, and in addition all the fibers, myelinated and unmyelinated, increase in diameter.

In the third phase growth in the diameter of the formed fibers is the most important factor, and this apparently continues so long as the brain increases in weight.

2. The second question touched the relation between the growth of the callosum and the psychological development of the rat. As we ascend in the mammalian series the relative importance of the callosum appears to increase.

Cameron ('17) says that in the lower orders of callosal mammals, where the surface of the cerebral hemisphere is smooth and free from convolutions, the corpus callosum is feebly developed, whereas in the higher orders, where the hemispheres show a progressive increase in the amount of the convoluting of gray matter, there is a concomitant increase in the size of the corpus callosum.

To make this comparison between man and the rat, table 7 has been prepared. According to the data there presented, the area of the cross-section of the callosum in man is 4.43 per cent

TABLE 7

Giving a comparison of the relations between the area of the total brain and the callosal area in man and in the albino rat. The data in columns A, B, C, D, are derived from Spitzka ('07) and the data in columns F, G, H, I, are derived from the records in table 3

MAN					ALBINO RAT				
Adult age 21-75 years	Area of				Adult age 70-378 days	Area of			
	Brain weight	Total brain	Corpus Callosum	$\frac{D}{C}$		BRAIN WEIGHT STANDARD	Total brain calculated	Corpus callosum-calculated	$\frac{I}{H}$
A	B	C	D	E	F	G	H	I	J
	grams	mm. ²	mm. ²	per cent		grams	mm. ²	mm. ²	per cent
10 ordinary men...	1443	12,770	562	4.44	9	1.836	149.9	4.93	3.29

of the computed area of the brain, while in the rat it is only 3.29 per cent. These figures show a clear difference in this relation, although the difference is perhaps not so large as we might have expected. Nevertheless, it may correspond in a general way to the relative proportions of the area of the cortex in the two species.

From my own studies on the ontogeny of the callosum I can conclude that there is also a progressive increase in the area of the corpus callosum with increasing body weight and age. The callosal area continues to grow until late in life, and in association with the increase of psychical activity, also to become more mature. I have already stated that from the twentieth

to the thirtieth day the growth rate of the callosal area is faster than before. This is very interesting because, according to Watson ('03), the first phase of psychical maturity is reached at this early age.

As part of our second question was the query whether there is any correlation between the increasing complexity of the psychical life and the number of the myelinated fibers in the callosum during its postnatal growth. In approaching this problem it is necessary to consider, 1) the method most suitable for myelin staining and, 2) the age at which the myelinated fibers first appear in the callosum.

After a number of experiments on the most suitable myelin stain, I chose the Kultschitzky-Wolter's method. This method seems to be the best for showing the very fine fibers and succeeds when the Pal-Weigert method almost fails, especially in the cross-sections. The material thus treated even at birth comes out quite clearly, and numerous unmyelinated fibers can be seen as brown rings.

At five days of age the callosum is almost unmyelinated. Here and there we find scattered blue points which at most indicate incompletely myelinated fibers.

An examination of the sections at seven days of age showed individual variations. The sections from two rats of this age showed almost no myelinated fibers, while the sections from the third rat at the same age showed a few scattered myelinated fibers. At this age the myelinated fibers begin to appear mainly in the dorsal portion of the callosum.

At the tenth day a few myelinated fibers can be seen here and there comparable to those found in the best-developed rat at seven days of age. Sections of this region from rats at twelve, fifteen, seventeen and twenty-two days of age showed a steady increase in number of myelinated fibers. Small ('99) says that memory is developed soon after ten days of age. At nineteen days after birth memory is well developed, while from birth up to twelve days of age the instinctive reactions are characteristic (Watson, '03).

By the twenty-fifth to the twenty-seventh day after birth there has been a distinct advance over the condition just described. The callosum now has myelinated fibers evenly distributed over its entire cross area, but these fibers are not yet as closely packed nor as darkly stained as those found in the mature callosum.

Although I have not counted the exact number of myelinated fibers in the callosum at different ages, it may be said safely that the increase of the callosal area is accompanied by an increase in the number of the myelinated fibers with increasing age.

We may conclude, therefore, that the increasing complexity of psychical response is associated with an increasing number of myelinated fibers in the callosum at least during the first two phases of its growth. After the thirtieth day of age all the myelinated fibers in the section stain as darkly as those in the sections from the adult rats.

Passing to the sections of the callosum from the adult rats, we find that in them the fibers are very closely packed together and darkly stained. Just when new fibers cease to appear in the callosum of the rat is difficult to determine.

I am particularly interested in the fact that the psychical development of the white rat runs about parallel with the increase in the number of the myelinated fibers in the sagittal callosal area, as is given in table 8—although of course I recognize that this is but one system of neurons and only a fraction of the entire brain—in which corresponding changes are also in progress.

3. Our third question related to the growth of the area of the cross-section of the callosum in the rat as compared with the corresponding growth change in man.

Unfortunately, a comparison between the rat and man in regard to the area of the callosum in sagittal section can hardly be made, owing to the absence of suitable data for man. The human callosal area at thirty-three years (mean age of ten ordinary men) has a mean value of ca. 563 sq.mm. (Spitzka, '07), but no record is given for the area at birth.

If the callosum of the rat brain at five days of age is similar in development to that of man at birth, and the growth processes in the rat are thirty times as rapid as in man, then the stage of completion of the callosal growth which occurs in the rat brain at about twenty-five days should occur in the human brain at about twenty months of age. This conclusion has not yet been tested.

TABLE 8

Showing the relation between development of the myelinated fibers in the callosum and the psychical development of the albino rat

AGE	DEGREE OF MYELINATION OF CALLOSAL FIBERS	GROWTH OF MYELINATION OF CALLOSAL FIBERS	PSYCHICAL DEVELOPMENT		
			Instinct	Memory	Psychical maturity
<i>days</i>					
Birth	—	Brown stained	Instinctive reactions are characteristic up to the 12th day		
5	—	Almost unmyelinated. Here and there can be seen incomplete myelin fibers			
7	—	Some sections show scattered myelinated fibers			
	+				
10	+	Scattered myelinated fibers		After this age memory develops	
12	++	Increase in number of myelinated fibers			
15	++	Increase in number of myelinated fibers			
17	++	Increase in number of myelinated fibers			
20	++	Increase in number of myelinated fibers		At 19 days perfect	
22	++	Increase in number of myelinated fibers			
25	+++	Myelinated fibers evenly distributed over its entire extent			
27	+++	Myelinated fibers evenly distributed over its entire extent			
30	+++	Darkly stained			

The data on the 'psychical development' are derived from the tabulation by Allen ('04) based on the data of Small and Watson.

SUMMARY

Employing sagittal sections, the corpus callosum from seventy-six albino rats, prepared from material fixed and stained by a uniform technique, we have obtained the following results:

1. In the albino rat the callosum at birth contains no myelinated fibers. These first appear from the seventh to tenth day and then increase rapidly in number and size.

2. The area of the callosum as shown in cross-section in the sagittal plane increases between birth and maturity about 3.5 times.

3. This increase occurs in three phases—an early phase, comprising the first ten days of life, in which new unmyelinated axones are added, while those already present increase in diameter. A second phase from the tenth to the thirtieth day, during which the formation of new myelin sheaths is the main factor, and a third phase after the thirtieth day, during which the increase in the diameter of the fibers is the most important change. Like the peripheral nerve fibers, these central fibers appear to increase in diameter so long as the brain increases in weight.

4. When during growth the thickness of the callosum is measured at the genu, truncus, and splenium, it is found that the proportional growth is greatest at the genu and least at the splenium. Thus the growth change is most marked at the frontal end of the callosum and diminishes toward the occipital end.

5. This series of growth changes represented by the three phases correlates very well with the psychical development of the rat—which is naturally a consequence of the maturing of the entire brain—of which the callosum is a part.

6. With the present data it is possible to compare the development of the callosum in man and the rat only at maturity. The comparison shows that the relative area of the callosum in man is distinctly greater than that in the rat—man 4.44 per cent, rat 3.29 per cent.

7. Using the method of equivalent ages as a basis for comparison, we should expect to find the fibers in the callosum of man well myelinated at the age of twenty months.

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Los núcleos motores de los nervios cerebrales en la Filogenia.
Un estudio de los fenómenos de neurobiotaxis.

III. Reptiles.

En la parte descriptiva del presente trabajo se describen detalladamente la morfología y relaciones de los núcleos motores y raíces de los nervios cerebrales de *Damonina subtrijuga*, haciéndose comparaciones con los resultados obtenidos en representantes de los diversos órdenes de los reptiles y con los anfibios. En la discusión se indica que el núcleo motor común y el aislado de los nervios VII-IX, que aparentemente constituyen un carácter del grupo de los reptiles, debe relacionarse probablemente con el divorcio de los efectores del glosofaríngeo y la acción respiratoria primaria, habiéndose desarrollado bajo la influencia del centro gustativo de los nervios VII-IX. La porción rostral del núcleo del hipogloso de los reptiles se ha originado bajo la influencia refleja del último centro y también la del núcleo terminal del ramo lingual del quinto nervio, que aparece por primera vez en la filogenia en los reptiles. Además, a juzgar por las pruebas acumuladas hasta el presente, es posible que la ausencia del núcleo accesorio en *Boa* no se debe primariamente a los cambios que siguen a la pérdida de la cintura escapular ofidiana. También se observa que las variaciones de las relaciones centrales del núcleo motor del quinto nervio de los reptiles pueden evidentemente relacionarse directamente con las especializaciones periféricas de la musculatura mandibular inervada por el nervio V. Finalmente, parece que la elaboración intrínseca del núcleo del oculomotor, evidente en ciertos reptiles, ha sido producida aparentemente como respuesta a la necesidad especial de la fijación ocular, debida al desarrollo de la retina en estas formas hasta alcanzar un punto de máxima agudeza visual.

THE MOTOR NUCLEI OF THE CEREBRAL NERVES IN PHYLOGENY—A STUDY OF THE PHENOMENA OF NEUROBIOTAXIS

III. REPTILIA

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INTRODUCTORY

The following communication represents part 3 of a series of papers dealing with the phylogeny of the cerebral motor nuclei in vertebrates, the first two parts of which were published in 1917 (4, 5). The delay in the progress of the investigation since that time has been unavoidable.

Most of the work in connection with the literature bearing upon the subject of this paper was carried out in the library of the University of Toronto, and it is a pleasure to acknowledge my indebtedness to Profs. B. A. Bensley, J. J. R. Macleod, and J. J. Mackenzie, of that institution, for their courtesy in placing the facilities of their departmental libraries at my disposal. I am also indebted to Prof. H. M. Evans for similar courtesies extended to me at Berkeley, California.

Damonia subtrijuga, which is here described in comparison with other reptiles, is a member of the cosmopolitan family Testudinidae.¹ This little tortoise is an Asiatic form occurring in Siam, Cambodia, and Java (Flower, 15). It is almost wholly aquatic in its habit and carnivorous in its diet.²

The motor nuclei and roots have already been studied and reconstruction charts have been made on the following reptilian types: *Chelone mydas*, *Alligator sclerops*,³ *Boa constrictor*, and *Varanus salvator* (see especially Kappers, 31, 32). These charts are reproduced for comparison in the present paper in figures 11 and 12, pages 82 and 83.

MOTOR ROOTS AND NUCLEI IN *DAMONIA SUBTRIJUGA*

Nerve XII

The hypoglossal roots in *Damonia* arise from a nucleus of large multipolar cells situated in the dorsal part of the rostral end of the gray reticulum of the cervical motor column. The majority of the cells comprising this nucleus lie rostrad of the exit level of the first hypoglossal rootlet. They form a cell

¹ Nomenclature according to Boulenger (6). Previous to the latter's work on the classification of *Chelonia*, Günther (23) has described this form under the name *Emys macrocephala*, while Gray (22) had recorded its occurrence under the name *D. macrocephala*, giving as synonyms *Geolemmys macrocephala*, Gray, and *Emys trijuga*, Mus.

² In captivity the animals observed by Flower (l. c.) refused all food except molluscs.

³ It is possible that the generic name *Alligator* has been applied to this specimen in mistake for *Caiman*. *C. sclerops* has a wide distribution from southern Mexico to northern Argentina and resembles *Alligator* in most features (Gadow, 13, and Cope, 10).

column as in *Rana catesbiana*, the limits of which are sufficiently well defined to enable it to be indicated diagrammatically in figure 11, C. The intrinsic differentiation of this cell group in *Damonia* presents little or no advance over the condition obtaining in *Rana* (5, figs. 1 and 2).

From their nucleus of origin the XII rootlets in *Damonia* take a curved course caudoventrad to emerge on the ventral periphery of the medulla, exhibiting in transverse section much of the appearance of the hypoglossal roots of higher forms (fig. 1). The foregoing description is one generally applicable to the XII root of reptiles, since in these forms the amount of white reticular substance incorporated in the floor of the medulla is greater than that characteristic of the Ichthyopsida (Kappers, 32).

The differentiation of a hypoglossal cell group in the rostral end of the cervical motor column is not so evident in *Chelone* as in *Damonia*. The same may be said with regard to this region in *Testudo* (Lubosch, 34), *Alligator*, *Varanus*, and especially *Boa* (Kappers, 32), though de Lange has observed a more highly specialized XII cell arrangement in *Chamaeleon* (Kappers, 33, p. 42) and Gisi has described a definite but small-celled XII nucleus in *Hatteria* (20, p. 180).

With regard to the incomplete separation of the hypoglossal nucleus from the rostral cervical motor column in reptiles, it is of interest to note that Willard has found a constant admixture of cervical and hypoglossal fibers in the last hypoglossal root in *Anolis*, though the more rostral rootlets of this nerve were composed entirely of hypoglossal fibers (43, p. 88). In *Varanus*, on the other hand, according to Watkinson (42, p. 467), the cranial element of the hypoglossal nerve which results from the union of three XII rootlets is only joined by the cervical elements outside the cranium.

Nerve X

In *Damonia* the vagus nucleus is dorsally situated, lying for the most part in the periependymal gray matter ventrolateral to the sulcus limitans (fig. 2). Rostrally it begins a short distance in front of the first X motor rootlet, and extends caudally to the

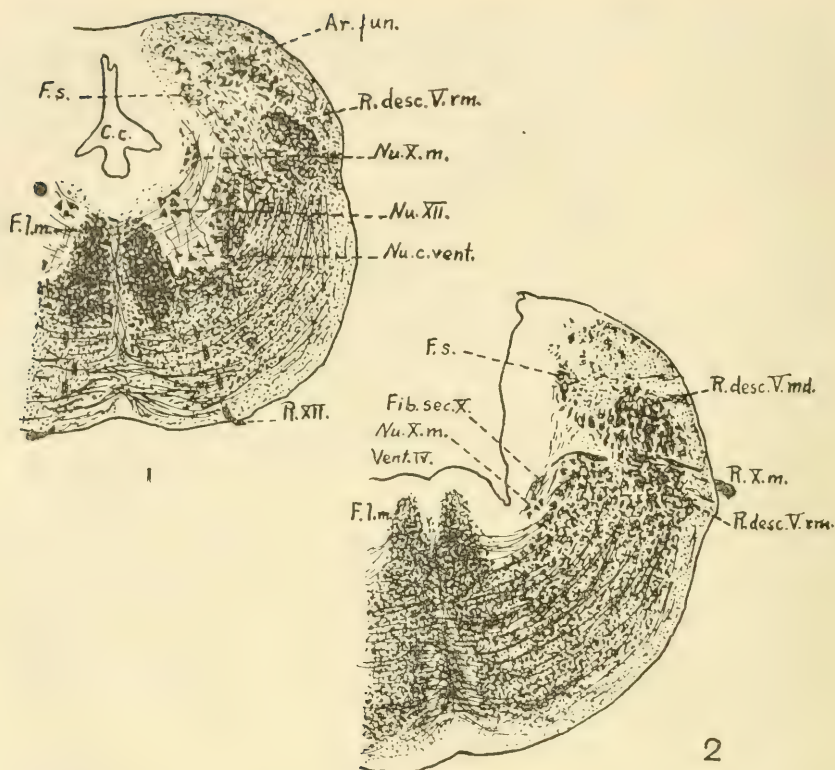


Fig. 1 *Damonia subtrijuga*. Transverse section through medulla just caudal of the calamus. Abbreviations: *Ar. fun.*, funicular area; *C.c.*, canalis centralis; *F.l.m.*, fasciculus longitudinalis medialis; *F.s.*, caudal extension of fasciculus solitarius; *Nu. c. vent.*, nucleus cornu ventralis; *Nu. X. m.*, motor vagus nucleus; *Nu. XII.*, nucleus hypoglossus; *R. desc. V. rm.*, descending trigeminal root chiefly composed of fibers from the ophthalmic and maxillary divisions (rostromaxillary) of this nerve (V. Valkenburg, 40); *R. XII.*, hypoglossal rootlet.

Fig. 2 *Damonia subtrijuga*. Transverse section through the medulla near the rostral end of the motor vagus nucleus. Abbreviations: *Fib. sec. X.*, secondary vagus fibers from the dorsal visceral nucleus (Kappers, 33); *F. s.*, fasciculus solitarius and associated gray which is of considerable size at the level (the descending nature of the fasciculus is more apparent here than at the same level in *Amphibia*); *R. desc. V. md.*, descending trigeminal root chiefly composed of mandibular fibers, many of which terminate in gelatinous gray abutting upon the visceral sensory VII-IX area (V. Valkenburg, l. c.); *R. X. m.*, vagus motor rootlet; *Vent. IV.*, fourth ventricle. Other abbreviations as before.

level of the second cervical segment. In the middle third of its extent the nucleus becomes enlarged by the addition of a number of cells along its ventrolateral periphery. Caudally this nucleus forms a small but well-marked cell column which can be traced through the first cervical segment. At this level its continuity is interrupted and it becomes represented by scattered cell clusters so that its exact caudal limit is ill defined. These relations are illustrated diagrammatically in the reconstruction chart, figure 11, C.

The fibers arising in the motor X nucleus pass first dorsad and then laterad in a curved course and emerge through the radix spinalis trigemini upon the dorsolateral periphery of the medulla.⁴ The caudal rootlets of this series emerge on a slightly more ventral plane than those described by Lubosch (34) in *Testudo*.

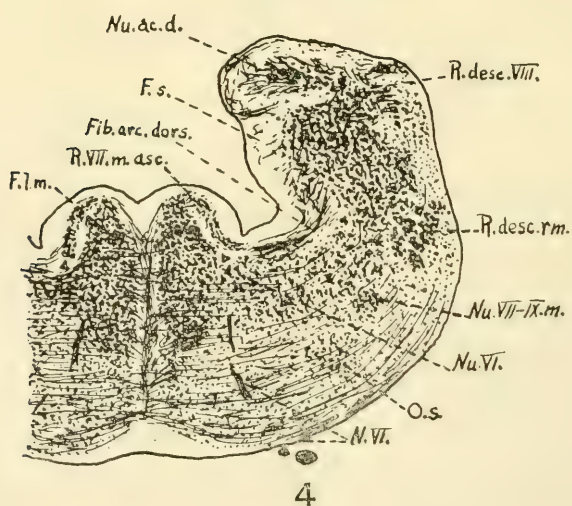
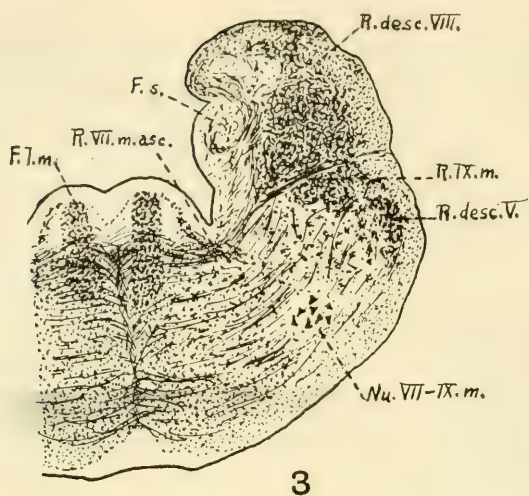
The arrangement of the elements of the motor vagus nucleus in *Damonia* closely corresponds to that obtaining in *Chelone*. In both these forms the motor vagus nucleus in the middle third of its extent is characterized by the presence of an accumulation of motor perikaryons on its ventrolateral periphery. The broad base of this flap-like cellular appendage is throughout its extent in direct continuity with the dorsal motor vagus column, and no subdivision into dorsal and ventral moieties occurs in these forms (fig. 11, C and D).

A more specialized condition obtains in *Varanus* and *Alligator*, where the differentiation of a lateral (ventrolateral) motor vagus cell group is clearly evident (fig. 12, A and C).

The apparently simple arrangement of the motor vagus column characteristic of *Boa* is possibly the direct result of the loss of certain motor vagus elements as a consequence of ophidian specialization, as Kappers has already noted (fig. 12, B). This question will be discussed subsequently.

The motor vagus column extends rostrally to the same relative level in all the reptiles thus far examined, irrespective of the

⁴ Fibers from some of the rostral vagus rootlets in *Damonia* terminate in the radix spinalis trigemini in a manner similar to that noted by Kappers in *Chelone*, *Alligator*, and *Varanus* (32, 33). In *Anolis*, on the other hand, Willard found no cutaneous components in any of the nerves between V and the third spinal (43).



order to which they belong. Thus it will be seen that the distance between the exit level of the caudal border of the VII motor root and the rostral end of the motor vagus nucleus is practically identical in the reconstruction charts (fig. 11, C and D; fig. 12, A, B, and C).

Furthermore, in contrast to amphibians, a wide interval exists in reptiles between the rostral end of the vagus motor column and the exit level of the motor IX root (fig. 11, A, B, C, and D).

In all the reptiles examined, with the exception of Boa, a condition obtains in the caudal part of the motor vagus column essentially similar to that described in *Damonia*. Thus, in *Testudo* (Lubosch), *Chelone*, Alligator, and *Varanus* (Kappers) the motor vagus nucleus extends well into the cervical region and the distribution of cells toward the termination of the column tends to be irregular.

Nerves VII and IX

In *Damonia* the motor root of nerve IX takes its origin in the caudal portion of a nucleus common to it and the motor VII root. This nucleus is situated in the ventrolateral reticular substance of the medulla, and its chief bulk lies caudad of the exit level of the motor IX root (figs. 3, 4 and 11, C). The

Fig. 3 *Damonia subtrijuga*. Transverse section through the medulla at the exit level of the motor glossopharyngeal root. Abbreviations: *F. s.*, visceral sensory area in which the descending fibers of the fasciculus solitarius are evident; *Nu. VII-IX. m.*, frontal end of the combined facial and glossopharyngeal motor nucleus; *R. VII. m. asc.*, facial motor root fibers passing dorsomedially from their nucleus of origin to the position in relation to the posterior longitudinal bundle which they occupy in their ascending course; *R. desc. VIII.*, descending vestibular root fibers; *R. IX. m.*, emergent motor glossopharyngeal fibers. Other abbreviations as before.

Fig. 4 *Damonia subtrijuga*. Transverse section through the medulla at the exit level of the last abducens rootlet. Abbreviations: *Cb.*, cerebellum; *F. s.*, upper end of visceral sensory column; *Fib. arc. dors.*, dorsal arcuate fibers of the octavomotor system passing to the abducens nucleus and posterior longitudinal bundle; *Nu. ac. d.*, dorsal acoustic nucleus; *Nu. VI.*, scattered large cells of abducens nucleus; *Nu. VII-IX. m.*, frontal tip of combined facial and glossopharyngeal motor nuclear area; *N. VI.*, abducens nerve rootlets; *O. s.*, area in which the scattered cells of the poorly differential superior olive are situated; *R. desc. VIII.*, descending VIII fibers.

emergent fibers of the IX motor root course first dorsomedial mingled with fine radicular VII motor root strands to the perpendymal gray beneath the sulcus limitans. In this region they course rostrad and, becoming separated from the more medially placed VII motor root fibers, pass dorsolaterad in an arched fashion through the *fibrae arcuatae dorsales*. At this point the root fibers form a compact bundle which makes its exit from the brain stem through the *radix spinalis trigemini* in a wide curve, the convexity of which is directed rostrad.

There is no line of demarcation between the cell groups giving rise to the motor VII and IX nerves. The caudal portion of the motor VII-IX nuclear complex is to be considered chiefly as the source of motor IX fibers and has been so illustrated in the reconstruction chart 11, C, because IX root fibers were traced to this center. It is to be understood, however, that all the fibers arising in this portion of the nuclear complex do not emerge in the motor IX root, for undoubtedly VII motor fibers arise here also. The rostral and by far the greater part of this nuclear mass is apparently wholly motor facial in character.

The motor VII root in *Damonia* arises in the VII-IX motor nucleus and takes a characteristically indirect course to reach its place of exit from the brain stem. The fine radicular fibers pass first dorsomedial and become collected upon the dorsal and lateral surfaces of the *fasciculus longitudinalis medialis* to form the ascending motor facial root. At a level somewhat rostrad of the plane of its exit⁵ the ascending root bends laterad and caudad, forming a well-marked genu. From the genu the emergent fibers pass laterad and caudad and pierce the *radix spinalis nervi trigemini* to make their exit on the lateral surface of the medulla (fig. 5).

With regard to the origin and course of the motor VII root, the relations described in *Damonia* correspond closely with those already worked out by Kappers in *Chelone*, *Varanus*, *Boa*, and *Alligator* and described by Gisi (20) in *Hatteria*. Such differ-

⁵ In figure 12 the level at which the genu of the motor facial root is formed is indicated on each reconstruction chart by the small vertical parallel lines rostrad of the exit level of the root in question.

ences as obtain are essentially those of degree and not of plan. The same may be said with regard to the motor IX root, where my observations on *Damonia* confirm those of Kappers on other reptiles in tracing the origin of this nerve to a nucleus common to it and the motor VII root.⁶

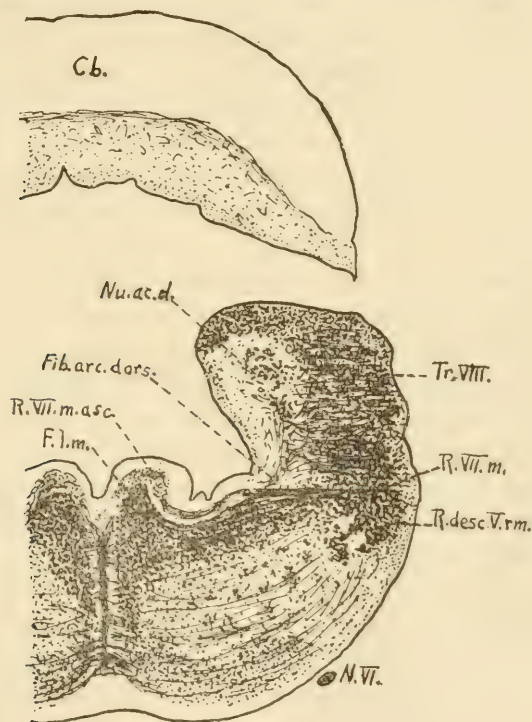


Fig. 5 *Damonia subtrijuga*. Transverse section through the medulla near the exit level of the motor facial root. Abbreviations: *Fib. arc. dors.*, dorsal arcuate fibers of the octavomotor system; *N. VI.*, abducens nerve; *R. VII m.*, emerging motor facial root; *R. VII m. asc.*, ascending motor facial root fibers cut both transversely, dorsal to the posterior longitudinal bundle, and obliquely, lateral to this structure; *Tr. VIII.*, acoustic tract and entering fibers. Other abbreviations as before.

⁶ Willard (l. c.) makes mention of his inability to make out the central relations of the motor VII and IX roots in *Anolis*, since his technique was designed primarily to stain peripheral structures. In view of the observations recorded above, it is to be expected that the central relations of these roots in *Anolis* will be found to conform to the general reptilian pattern.

It is probable that in Hatteria the origin of the motor IX root is similar to that obtaining in other reptiles. The glossopharyngeal motor root in this form arises by three fine rootlets close behind and somewhat more ventrally placed than the acusticus root (Gisi, l. c., p. 179). Some of the fibers of this nerve are said to arise in a small nuclear area ventral from the descending acusticus root and would appear from the description to be sensory in character. Other fibers of the IX nerve are described as being evidently connected with the fasciculus longitudinalis medialis, and these no doubt represent the motor component. Gisi also observes that the motor VII nucleus, made up of numerous groups of cells, extends caudally for a long distance in this animal.

A comparison of the reconstruction charts (figs. 11 and 12) brings out the fact that among the reptiles examined the motor VII-IX nuclear complex with reference to the exit level of the motor VII root is most rostrally placed in Alligator and most caudally situated in Damonia, Varanus, Boa, and Chelone, occupying intermediate places, respectively, in a scale arranged on this basis of comparison. Further, when compared as to their position with regard to the floor of the fourth ventricle, the most dorsally situated complex is found in Alligator, Chelone, Boa, Damonia, and Varanus following in the order named. Finally, it is to be noted that a small ventral motor VII nucleus is present in Alligator as well as a third cell group labeled in figure 12, A, with a question mark (?) whose connection with the motor VII root has not been fully established. These subsidiary cell groups have not been observed in the other reptiles examined, though a partial division of the motor VII-IX nucleus into dorsal and ventral moieties is indicated in Varanus (Kappers, 31, p. 65).

Nerve VI

In Damonia the abducens nerve arises in an elongated and somewhat diffusely arranged nucleus of large multipolar cells lying in the reticular formation alongside the fasciculus longitudinalis medialis and in intimate association with the fibrae

arcuatae dorsales. In this dorsal situation the nucleus extends from a short distance behind the caudal border of the emergent motor VII root to a point slightly rostrad of the exit level of the IX motor root. The abducens fibers course ventrad and slightly laterad to reach the periphery, where they emerge as three fine rootlets in linear series between the exit levels of the motor VII and IX roots (figs. 4 and 11, C).

A comparison of the reconstruction charts B and C in figure 11 shows that a striking similarity exists in the topographical relations of the abducens roots and nucleus in *Damonia* and *Rana catesbiana*.

In reptiles, as Kappers has pointed out, the abducens nerve is subject to considerable variation both in the number and place of exit of its roots as well as in the topographical relations of its nucleus. Thus in *Alligator* eleven rootlets are present, three of which emerge caudad of the motor IX root; in *Chelone* six rootlets are present, the most caudal of which emerges at the exit level of the motor IX root; in *Damonia* six rootlets are present as described above; in *Anolis carolinensis* several rootlets, the number of which is not given, emerge at the same relative level as in *Damonia* (Willard, l. c., p. 45 and pl. 2, fig. 4); in *Boa* the six rootlets all emerge rostral of the exit level of the motor VII nerve; in *Varanus* five rootlets are present, of which the first three are very close together and the last two are very small, all of them emerging rostrad to the exit level of the motor VII root. The corresponding variations in nuclear topography will be described in connection with the subsequent discussion.

In *Hatteria* the abducens nucleus consists of a somewhat scattered cell group lying lateral and dorsal to the fasciculus longitudinalis medialis (Gisi, 20, p. 178). Its emergent fibers form four or five rootlets upon the ventral surface of the brain stem, but Gisi does not note their relation to the exit level of the motor VII root.

Nerve V

In *Damonia* the motor V root arises in a dorsally situated large-celled nucleus and its emergent fibers course in a direct manner lateroventrad to reach the periphery of the brain stem ventral to the entering sensory V root as in *Rana* (fig. 6). The chief bulk of the nucleus lies on the level of its root exit, a small portion only extending rostrad of this plane and none of its cells being found below the level of the caudal border of its emergent root (fig. 11 C).

In figure 6 the motor V root is seen to be separated by a slight space from the more dorsally placed incoming fibers. Among the latter may be distinguished the mesencephalic V root which pursues its course from this level to its nucleus of origin in the midbrain in a manner essentially similar to that already described by Van Valkenburg in *Chelone* (39 and 41). The mesencephalic V root in *Chelydra* has also been figured though not described by Humphrey (28, pl. III, fig. 21), who refers, however, to Herrick's earlier description of this root in reptiles (24, p. 138).

As in *Chelone*, the caudal part of the motor V nucleus in *Damonia* is most ventrally situated, though no indication of an isolated ventral motor V nuclear moiety is to be seen in the latter form. *Damonia* differs from *Chelone*, however, in the smaller relative size of its motor V nucleus and in the rostral position of this nucleus with reference to the exit level of the motor V root (fig. 11, C and D).

The arrangement of the cells of the motor V nucleus in *Alligator* resembles in general that in *Chelone*. In *Alligator* (fig. 12, A), however, this nucleus is much more caudally placed with reference to its root exit and the ventroperipheral moiety is more distinct than in *Chelone*. In *Boa* and *Varanus* (fig. 12, B and C) a still more extensive development of the ventroperipheral portion of the motor V nucleus is evident, and no part of the nucleus in these forms occupies such a dorsal position as does the chief bulk of the motor V cell group in *Alligator* (Kappers, 31, 32).

In *Anolis* Willard has described in detail the central origin of the motor V root which in this form is arranged on a plan somewhat similar to that obtaining in *Varanus*. In the former

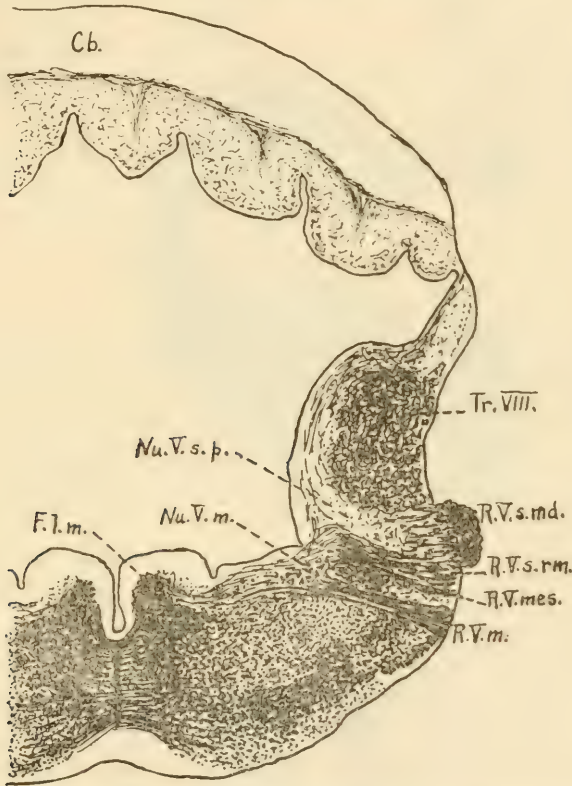
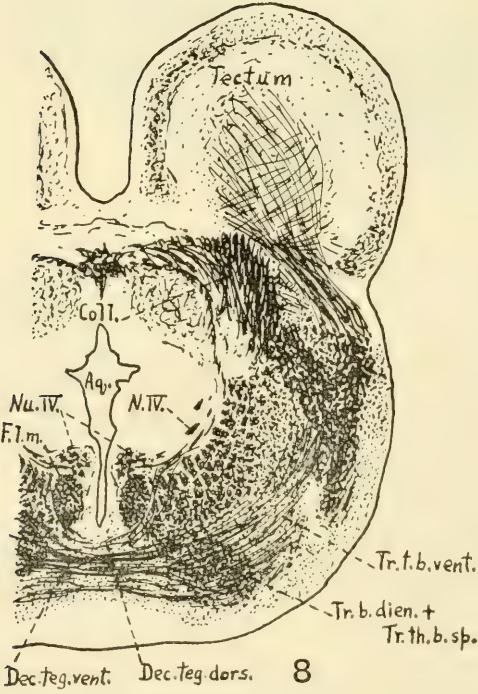
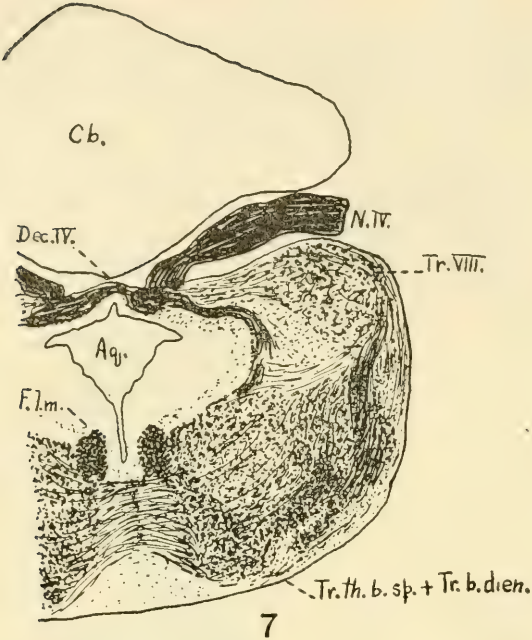


Fig. 6 *Damonia subtrijuga*. Transverse section through the medulla at the exit level of the motor trigeminal root. Abbreviations: *Nu. V. m.*, motor trigeminal nucleus; *Nu. V. s. p.*, so-called principal sensory trigeminal nucleus in which components from all three divisions of this nerve terminate near the level of their entrance; *R. V. m.*, motor trigeminal root; *R. V. mes.*, emergent mesencephalic trigeminal root fibers; *R. V. s. md.*, root fibers of the mandibular division of the trigeminus which enter the brain stem somewhat caudad of those of the ophthalmic-maxillary division, *R. V. s. rm.* (V. Valkenburg, l.c.); *Tr. VIII.*, area acustica alba. Other abbreviations as before.

animal the motor V root is described as arising from two cell groups, one of which is placed a short distance dorsomesiad of the peripheral attachment of the root, while the second occupies



a dorsal position just laterad of the fasciculus longitudinalis medialis. Both cell groups in this form were situated on a level caudad of the plane of exit of the motor V root (Willard, 43, p. 48, and Kappers, 31, p. 40).

In general it would appear from the material examined that the synapsid (*Damonia* and *Chelone*) and diapsid (*Alligator*) forms are characterized by the dorsal situation of most of the motor V perikaryons, while in the *Squamata* (*Boa*, *Anolis*, and *Varanus*) the chief bulk of the motor V nucleus is more ventrally or rather peripherally placed (figs. 11 and 12).

Nerves III and IV

In *Damonia* the trochlear nucleus lies in the Sylvian gray some distance rostrad of the level of its root exit. At this level the floor of the aqueduct is prolonged ventrad to form a deep sagittal fissure between the fasciculi longitudinales mediales (fig. 8). It thus happens that the trochlear nucleus which lies upon the dorsal aspect of each posterior longitudinal fasciculus is placed dorsad of the ventricular floor. It seems hardly necessary to add that in figure 11, C, the distance from the upper horizontal boundary line of the chart to the trochlear nucleus indicates the approximate distance of the nucleus in question from the ventricular cavity, not from the floor in the sagittal plane. The same condition holds true in regard to the reconstruction of the oculomotor nucleus. From its nucleus of origin

Fig. 7 *Damonia subtrijuga*. Transverse section through the brain stem at the exit level of the trochlear root. Abbreviations: *Aq.*, iter; *Dec. IV.*, trochlear decussation; *N. IV.*, trochlear nerve; *Tr. b. dien.*, tractus bulboencephalicus (de Lange, 12); *Tr. th. b. sp.*, Tractus thalamo-bulbo-spinalis whose fibers are intermingled with the preceding tract (De. Lange, l.c.); *Tr. VIII.*, secondary acoustic paths. Other abbreviations as before.

Fig. 8 *Damonia subtrijuga*. Transverse section through the brain stem at the level of the trochlear nucleus. Abbreviations: *Coll.*, caudal portion of colliculus; *Dec. teg. dors.*, decussation of dorsal tectobulbar system (de Lange, 11, 12); *Dec. teg. vent.*, decussation of ventral tectobulbar system; *Nu. IV.*, trochlear nucleus; *Tectum*, tectum opticum; *Tr. t. b. vent.*, arcuate bundles of the tractus tecto-bulbaris ventralis coursing ventromedial to decussate. Other abbreviations as before.

the trochlear root fibers pass laterodorsad and descend in the peripheral portion of the Sylvian gray. At the level of their exit the two roots converge abruptly and after decussating in the medullary velum, emerge upon the dorsal periphery (fig. 7).

The oculomotor nucleus in *Damonia* is situated in the gray matter of the midbrain floor. In transverse section it lies dorso-mediad of the faciculus longitudinalis medialis in the angle formed by this structure and the narrow midsagittal fissure of the iter which here extends to within a very short distance of the ventral periphery (fig. 9). The nucleus is composed of large multipolar cells resembling closely those of the trochlear nucleus and forming a fairly compact mass which is not divisible into subsidiary cell groups. The nucleus begins a few sections behind the level of the rostral border of the oculomotor root and extends for some distance below the level of the most caudal emergent fibers of this nerve. A considerable interval, however, separates the oculomotor cell group from the caudally situated trochlear nucleus (fig. 11, C).

The oculomotor root fibers pass ventrolaterad through the medial part of the faciculus longitudinalis medialis and between the bundles of the tractus tectobulbaris dorsalis cruciatus to reach the periphery on either side of the ganglion interpedunculare. No oculomotor fibers arising in the contralateral nucleus could be distinguished.

By the degree of their cellular differentiation and in their relations to the exit level of the oculomotor root, the III and IV nuclei and the trochlear roots are strikingly similar in *Damonia* and *Chelone*. It is significant also that *Boa* resembles both *Damonia* and *Chelone* in these relations, though in other respects presenting so marked a contrast to these forms.

In *Alligator* and *Varanus*, on the other hand, Kappers has shown that the oculomotor nucleus exhibits a relatively high degree of cellular differentiation, so that in these forms a dorso-lateral and ventromedian oculomotor cell group may be distinguished. A similar condition obtains in *Chamaeleon* (Kappers, 32, p. 63; de Lange, 12, p. 136).

In *Anolis* Willard notes that the trochlear nucleus and the whole central course of its root may be seen in a single transverse section (l. c., p. 45). The relations of the oculomotor root and nucleus are not so evident from his description, but it would appear that most of the nucleus is situated on the level of its emergent root. This being so, on reference to Willard's reconstruction (l. c., pl. 2, fig. 4), the fact emerges that a considerable

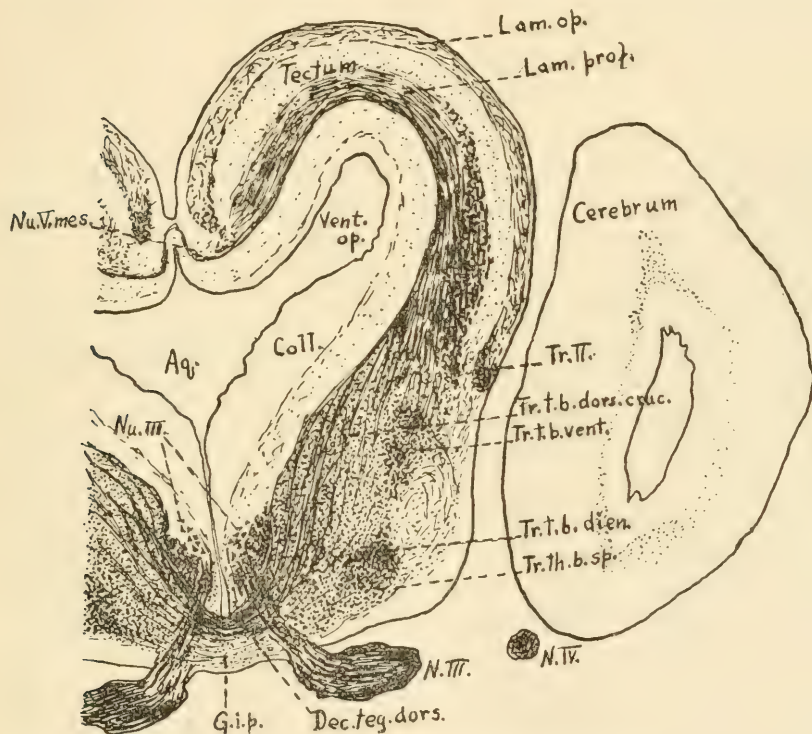


Fig. 9 *Damonia subtrijuga*. Transverse section through the brain stem at the level of the oculomotor root exit. Abbreviations: *G. i. p.*, ganglion interpedunculare; *Lam. op.*, afferent optic fibers to tectum; *Lam. prof.*, deep medullated lamina of tectum; *N. III.*, oculomotor nerve; *Nu. III.*, nucleus oculomotorius; *Nu. V. mes.*, cells of mesencephalic nucleus of trigeminus; *Tr. II.*, tractus opticus; *Tr. t. b. dors. cruc.*, arcuate bundles of the tractus tectobulbaris dorsalis cruciatus passing ventromedial through scattered bundles of the tractus tectobulbaris non-cruciatus to decussate; *Tr. t. b. vent.*, ventrolateral system of tectobulbar fibers before decussation; *Vent. op.*, optocoele. Other abbreviations as before.

interval must intervene between the caudal end of the oculomotor group and the rostral end of the trochlear nucleus in this form.

In the oculomotor nucleus of *Hatteria*, Gisi has described both dorsofrontal and ventrocaudal cell groups (20, p. 176). Further, she has noted that most of the caudal fibers of the oculomotor root in this animal arise in the contralateral ventral nucleus of this nerve.

DISCUSSION

1. *Hypoglossal complex*

In the preceding description it has been noted that differentiation within the hypoglossal nuclear area in *Damonia*, *Chelone*, *Alligator*, *Boa*, and *Varanus* has not reached a stage much in advance of that obtaining in opisthoglossal anurans.

Among the latter forms it has been shown that the differentiation of the hypoglossal cell group is definitely correlated with the development of the tongue as a muscular prehensile organ (5). In view of this, a relatively slight differentiation of the hypoglossal nuclear area might be expected in *Alligator* and in chelonians, since the tongue of these animals is non-protrusible. In *Varanus*, on the other hand, lingual movement is not so restricted, and in *Boa* the tongue is modified to form a highly specialized tactile organ. In neither of these forms, however, does the morphology of the hypoglossal nucleus show evidence of a higher state of differentiation than that obtaining in *Alligator*.

It is of interest to recall that the arrangement of the occipitospinal nerve roots in reptiles is on a plan more primitive than that obtaining in the Anura. In adult opisthoglossal anurans the first occipitospinal nerve ('a' of Fürbringer's table, 16) is missing and the fibers arising in the dorsomedial cell groups or XII nucleus of these forms are restricted in their exit to one ventral root, viz., that of the second spinal nerve ('b') of Fürbringer's, first of the adult series). On the other hand, all the roots of Fürbringer's occipitospinal series are represented in the reptiles under discussion so that the fibers arising in the rostral portion of the somatic motor column (dorsal cell group or hypo-

glossal nucleus) are thus distributed in their exit over a relatively wide area to three roots, viz., 'a,' 'b,' and 'c' of Fürbringer.

In one respect, viz., in its more rostral position in the brain stem, the hypoglossal nucleus of reptiles shows a marked advance over the condition obtaining in Amphibia. This fact is well known from Kappers' earlier investigations (l. c.) and may be clearly demonstrated by reference to figures 11 and 12, where it will be seen that the hypoglossal nucleus extends to within a relatively short distance of the rostral end of the motor X column and a condition obtains which foreshadows the more complicated relations characteristic of birds and mammals.

From these reconstruction charts it is evident that the distance between the caudal border of the motor VII root and the rostral end of the cervical motor column is much less in reptiles than in amphibians, and further that with regard to the character in question there is a remarkable degree of uniformity among the reptiles examined. That the marked difference of this measurement in reptiles and amphibians is not due to the persistence in the former animals of the motor roots of the rostral occipito-spinal nerves is further evident on comparing such forms as *Chelone* and *Triton*, in both of which the full number of these roots persist (Fürbringer, l. c.).

With regard to the influences which have contributed to the rostral migration of the XII nucleus in reptiles, the following facts are significant. In reptiles as in adult amphibians the distribution of gustatory sense organs is limited to the buccal and pharyngeal regions (Kappers, 33). In contrast to amphibians, however, the mucosa covering the rostral portion of the tongue is innervated by trigeminal fibers in reptiles, among whom for the first time in phylogeny the lingual branch of the trigeminal nerve appears (Kallius, 29, p. 748).

The nucleus of termination for the V lingual fibers is chiefly in the dorsal area of the substantia gelatinosa Rolandi, as Van Valkenburg has shown (40). This author has pointed out that the descending fibers of the mandibular division of the trigeminal root do not extend so far caudad as do those of the ophthalmic and maxillary roots, and further that the position and entity

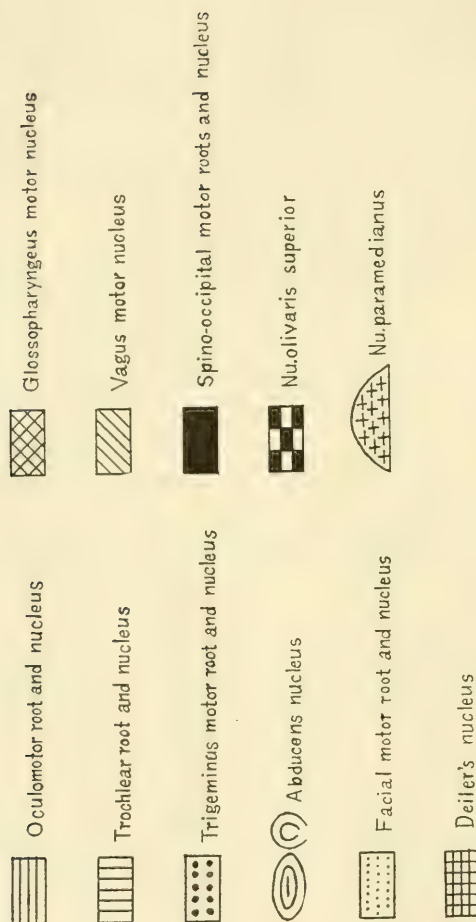
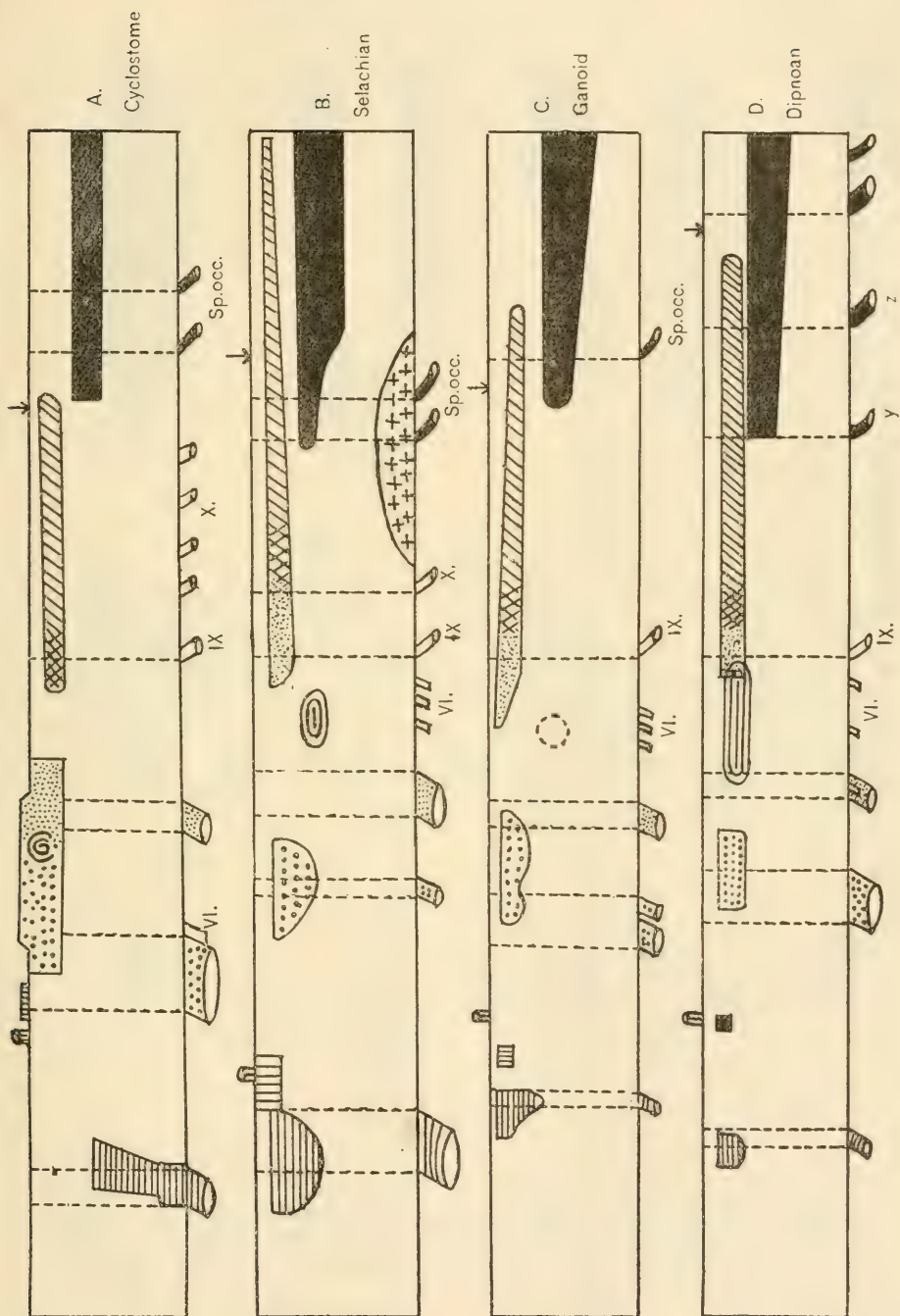


Fig. 10 Reconstruction charts of motor roots and nuclei in lower ichthyopsidans for comparison with figures 11 and 12. A, *Petromyzon fluviatilis* (after Kappers, 32); B, *Selache maxima* (4); C, *Polyodon spathula* (4); D, *Neoceratodus forsteri* (after Van der Horst, 38). Except for the caudal position of the trochlear nucleus in this form, the motor nuclear pattern in *Neoceratodus* is almost identical with that in the crossopterygians, *Polypterus* and *Calamoichthys* (Van der Horst, l. c.). Abbreviations: VI, abducens roots; IX, motor glossopharyngeal root; X, first motor vagus rootlet; y, z, and *sp. occ.*, spino-occipital rootlets. The arrow indicates the site of the calamus. See diagram above for explanation of signs.



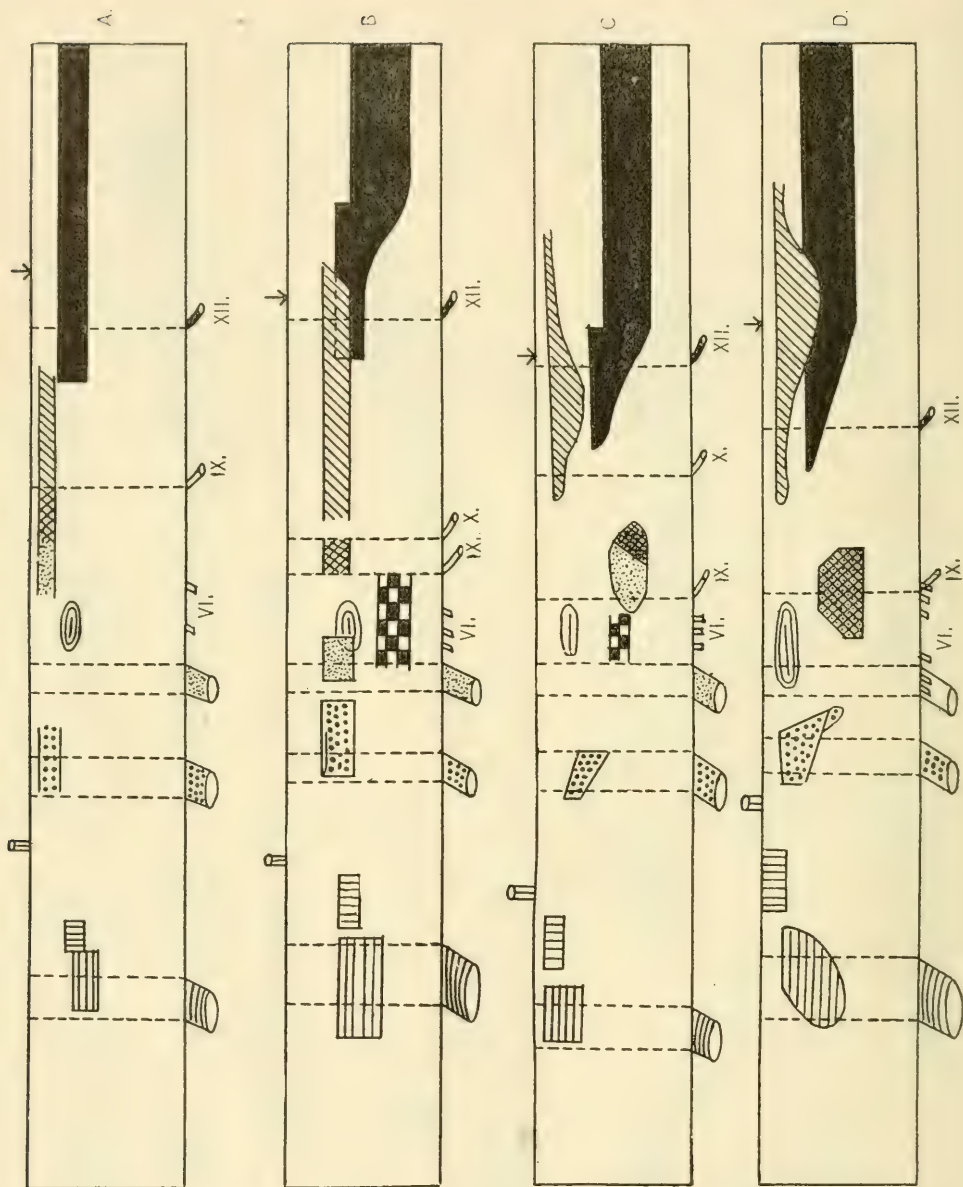


Fig. 11 Reconstruction charts of motor roots and nuclei. A, *Triton vulgaris* (after Kappers, 32); B, *Rana catesbiana* (5); C, *Damonina subtrijuga*; D, *Chelone mydas* (after Kappers, l. c.). XII., hypoglossus roots. Other signs and abbreviations as before.

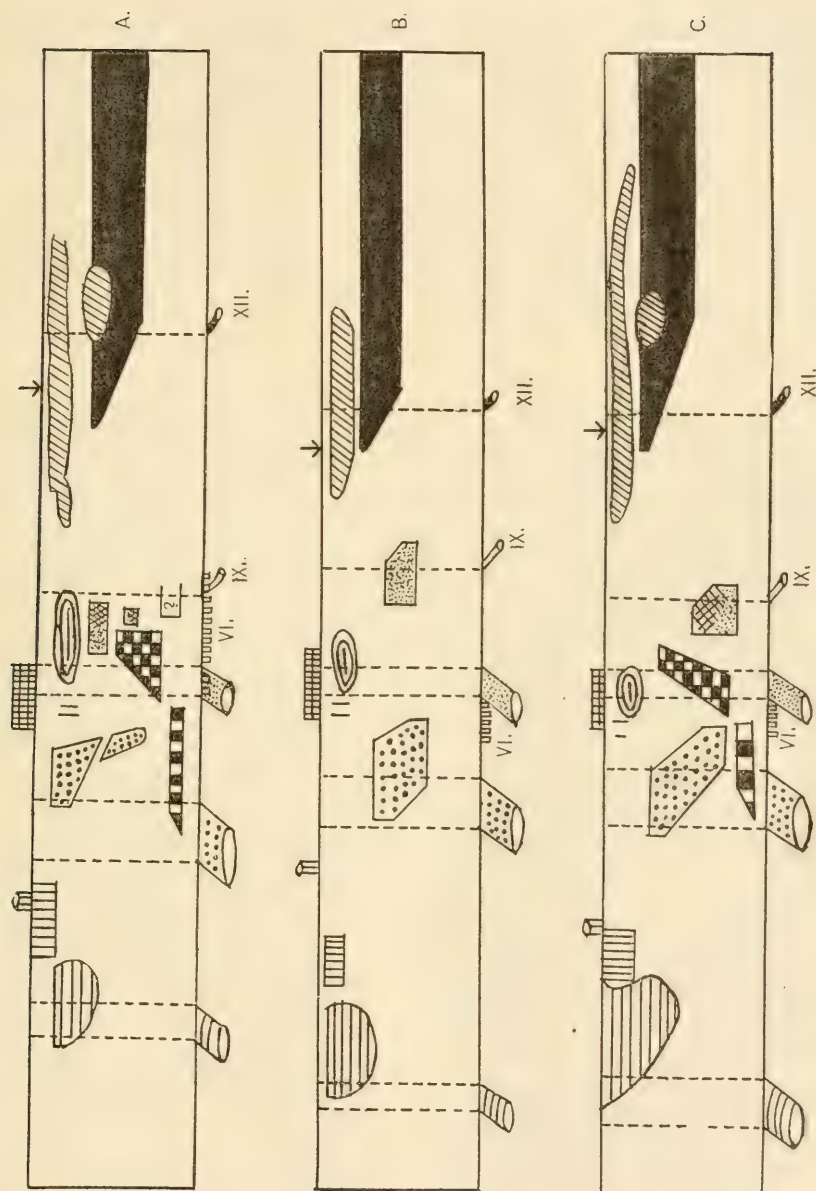


Fig. 12 Reconstruction charts of motor roots and nuclei. A, *Alligator sclerops* (footnote 3, p. 62); B, *Boa constrictor*; C, *Varanus salvator*. (All charts after Kappers, 32.) Signs and abbreviations as before.

of the dorsal mandibular moiety of the radix descendens trigemini is primarily determined through the influence of the terminal gustatory area. Thus in reptiles for the first time in phylogeny the reflex action of the musculature of the tongue may be initiated by impulses arising simultaneously in the lingual mucosa and reaching the medulla by way of both trigeminal and gustatory paths. The rostral position of the hypoglossal nucleus of reptiles is an expression of this important reflex influence in accordance with the first concept of neurobiotaxis (Kappers, 32).

2. *Visceral motor nuclei*

Vago-accessorius complex. In the foregoing description attention has been directed to the fact that the motor vagus column extends well into the cervical region as a small but definite nucleus in *Damonia*, *Chelone*, *Alligator*, and *Varanus*. In contrast to this, the motor vagus column terminates abruptly in the lower region of the medulla in *Boa constrictor*.

Fürbringer (16) has described the superficial origin, course, and distribution of the nervus accessorius (ramus accessorius X) in *Chelonina*. In these forms this nerve is somewhat variable in size and innervates the m. capiti-plastralis in common with the third and fourth cervical nerves. In *Crocodilia* Fürbringer (17) has also described a nerve homologous with the R. accessorius X of chelonians which was distributed to a small part of the m. sterno-mastoideus (viz., m. atlanti-mastoideus). In the *Crocodilia* this nerve by reason of its intimate connection with the cervical nerves shows a form and arrangement differing somewhat from that obtaining in chelonians. The superficial origin and course of the nervus accessorius in *Varanus* has been described by Watkinson (42, p. 467). The nerve in question was found to innervate the 'm. sterno-cleido-hyoideus' (= m. capiti-cleido-episternalis of Fürbringer, 17) in common with fibers derived from the third cervical nerve.

Among the snakes, on the other hand, Hoffmann (26) long ago pointed out that in correspondence with other specializations attendant on the loss of their limbs, a homologue of the R. accessorius X is absent.

In all reptiles in which it occurs, the R. accessorius X is formed by the union of the most caudal roots of the vagus series. Thus, in reptiles as in fishes (4) and amphibians (5) the central origin of the homologue of the accessory nerve of mammals must be represented by the caudal end of the motor vagus column.

In the earlier discussion of the homologues of the accessory nerve in ichthyopsidans (5, pp. 415-420) it was pointed out that the two elements (somatic and visceral) of the trapezius complex of higher forms might well be represented as discrete effectors in lower forms, but that a primitive prostadium of the typical sauropsidan condition might be looked for among the more generalized amphibians. Apparently such conditions obtain respectively among anurans in *Rana* and among urodeles in *Siren*.

At the time when the discussion alluded to above was published, I was under the impression then current that among reptiles, snakes alone were devoid of any vestige of a nerve homologous with the ramus accessorius vagi of mammals. The exact investigations of Willard have, however, brought to light the fact that in a saurian such as *Anolis*, which presents no very highly specialized features, the visceral component of the trapezius complex is entirely absent.

The somatic components of the muscular complex are well represented in *Anolis* where the m. episterno-cleido-mastoideus and m. capiti-dorso-clavicularis are, save in respect to their nerve supply, essentially similar in their relations and functions to the similarly named muscles of Hatteria and many of the Lacertae, to the m. capiti-sternalis and m. dorso-scapularis of the Chamaeleonidae, to the m. capiti-sternalis and m. dorso-scapularis of crocodiles and to the m. capiti-plastralis of chelonians (Fürbringer, 16 and 17).

Until recently it has naturally been supposed that the absence of the accessorius nucleus in snakes was a condition acquired subsequently to and consequent upon the loss of their shoulder-girdle and its visceral levator musculature. In the light of Willard's findings, the foregoing conception may require modification, for it is at least possible that in the forms ancestral to

ophidians no such visceral component of the trapezius complex was present.

In connection with my earlier observations on the probable phylogeny of the sauropsidan cucularis (5, p. 417) it is significant that a definitely developed homologue of the accessory nerve and trapezius complex in which somatic and visceral elements are inextricably blended, has been found in every synapsid and diapsid form so far examined, while variations away from this condition of development have only been encountered in reptiles belonging to the more modern group Squamata.

With regard to the ventrolateral X motor nucleus which appears for the first time in phylogeny in reptiles, Kappers has suggested the possibility of its representing a cardiac nucleus (32). On the other hand, it may possibly be correlated with the specialization of the vasomotor swell mechanism (m. constrictor venae jugularis of Bruner, 8) so characteristically developed among reptiles. However, further discussion of the significance of this cell group will be postponed until the homologous area of the brain stem of birds has been considered in a subsequent communication.

Motor VII-IX complex. The characteristic origin and course of the motor VII root in reptiles has been discussed at length by Kappers in his earlier papers (see especially 30 and 31). This author has shown that the pronounced frontal genu of the VII motor root in these forms is due for the most part to the restraining influence of the dorsal arcuate fibers from the tuberculum acusticum and especially those from the nucleus laminaris (Holmes, 27). The caudal genu of the root is the result of the ventrolateral migration of the nucleus from its original dorsal location. This displacement is most evident in *Varanus* and is less marked in *Damonia*, *Boa*, *Chelone* and *Alligator* in the order mentioned.

The degree of caudal migration of the motor VII nucleus in reptiles (i.e., the length of the horizontal root) has been shown by Kappers to be directly correlated with the size and importance of the terminal VII-IX gustatory nucleus. In chelonians the tongue is supplied with taste buds over the whole of its surface (Tuckerman, 37), while this organ is practically destitute of taste

buds in crocodilians. In the latter forms taste buds are said to occur only on the dorsal part of the mouth near the choanae and around the entrance of pharynx (Bath, 3). In correspondence with these peripheral conditions, the VII-IX motor nucleus is most caudally situated in chelonians (*Damonina* and *Chelone*) and most rostrally placed in Alligator.

The association of the motor VII-IX nuclei in reptiles to form a single cell complex is one of the most striking peculiarities of the motor nuclear pattern of these forms. A similar motor VII-IX nuclear association has been observed in such widely dissociated forms as *Lophius* and *Canis*, but in no vertebrate class other than reptiles does this condition obtain as a group character. It follows, therefore, that in each of the various reptilian orders some fundamentally similar reflex mechanism must exist whose common efferent path consists of VII-IX neurones.

It will be of interest to inquire whether or not there be any constant feature in the peripheral distribution of the motor VII and IX nerves which may suggest some reason for the central association of their motor perikaryons. Among reptiles it may be broadly stated that the VII motor nerve is distributed peripherally to three muscles, viz., m. depressor mandibulae, m. sphincter colli, and m. intermandibularis in its caudal part.⁷ On the other hand, the motor IX peripheral distribution in reptiles would appear to be somewhat variable. In *Anolis* Willard (l. c.) has called attention to the fact that the laryngeal muscles may be innervated from IX, from X, or from both these nerves. Göppert (21) considers that the R. recurrens vagi alone supplies the laryngeal muscles of reptiles. Hoffmann (l. c.) describes the muscles of the larynx as innervated by the IX in chelonians where this nerve is also distributed to the m. cerato-maxillaris and in crocodilians to 'pharyngeal muscles.' Thus, among reptiles it may be said that while the peripheral

⁷ This nomenclature has been somewhat arbitrarily selected from the host of synonyms by which these muscles have been known because it appears to be most generally descriptive of the muscles in question (Adams, 1; Willard, 43; Hoffmann, 26; Edgeworth, 13; Watkinson, 42; Fatamura, 14; Bradley, 7, et al.).

distribution of the motor VII nerve is relatively constant, that of the motor IX may be quite variable so that a simple consideration of the peripheral distribution of their nerves gives no hint of the possible underlying cause of the central association of their motor nuclei.

From the functional standpoint, however, facts may be adduced which seem to have some bearing upon this question. Among reptiles for the first time in phylogeny pulmonary ventilation may be carried on independently of the hyobranchial pump mechanism, so that in these forms, in contrast to amphibians, the glottis may remain open throughout the whole cycle of pulmonary respiration. Closure of the glottis is, however, necessary during deglutition in all reptiles, at least during the first stages of this act. During the whole cycle of pulmonary respiration in water-living reptiles (crocodilians and chelonians) the mouth may be kept open while the body is submerged with only the nostrils protruding above the surface. In such animals, therefore, closure of the glottis does not necessarily result through the stimulation of the buccal mucosa innervated by V and VII sensory nerves by water or food. Closure of the glottis does take place, however, when such stimulation reaches the mucosa of the VII-IX sensory area and when at the same time the buccopharyngeal muscles are called into play in the first stage of the act of deglutition. The same holds true of land-living reptiles, though in snakes the rima glottidis may be protruded between the two halves of the lower jaw and remain open during the much prolonged act of deglutition (v. Gadow, l. c.). Thus among reptiles for the first time in phylogeny the effectors supplied by the motor IX are no longer muscles of primary respiratory importance, but are called into play more especially during the act of swallowing immediately after or at the same time as the VII musculature and as the result of the same stimulation.

In *Rana* it was found that the complete separation of the motor VII nucleus from the closely related and caudally placed IX-X motor nuclei was apparently a central expression of the changed peripheral relations due to the divorce of the facial musculature from respiratory functions (5, p. 411). In urodeles the retention

of the selachian arrangement of the VII-IX-X visceral motor nucleus appeared to be an indication of the relative importance of the respiratory function of the hyobranchial musculature (5, p. 412). Similarly in reptiles it would seem that the central association of glossopharyngeal with facial motor perikaryons rather than with vagal elements may be due to a rearrangement of the visceral motor nuclear pattern largely as a consequence of the loss of the hyobranchial pump mechanism for pulmonary ventilation, and, as Kappers has shown (30, 32, 33), under direct influence of the caudal VII-IX taste center.

Motor V nucleus and root. With regard to the arrangement of the elements of the motor V nucleus the reptiles examined are evidently divisible into two distinct groups, to the first of which belong *Damonia*, *Chelone*, and *Alligator* and to the second *Boa* and *Varanus*.

In the first group the motor V nucleus is for the most part dorsally situated, but the cells in its caudal portion show a tendency toward ventral (peripheral) displacement, a process which in *Alligator* has resulted in the formation of a distinct caudoventral moiety of the nucleus (figs. 11, C, 11, D, and 12, A.)

It has been shown that in its primitive position the motor V nucleus in ichthyopsidans occupies a dorsal position on or near the level of its root exit (4, 5). Among reptiles the motor V nucleus has retained this primitive position to a large extent in those forms in which the differentiation of the jaw musculature is least advanced, viz., chelonians (Adams, 1, p. 89 et seq.).

Evidence of a greater degree of nuclear differentiation is to be seen in *Alligator* as noted above. It is significant, in view of this, that the m. capiti-mandibularis in this form in contrast to chelonians is further differentiated to form superficial, middle, and deep muscles, while the m. pterygoideus anterior is supplemented by the presence of a m. pterygoideus posterior not differentiated in chelonians (Adams, l. c.).

The distinction between the type of V nuclear arrangement obtaining in *Alligator* and chelonians is not fundamental, but one of degree only, and there can be little doubt that this is to be correlated with the essential similarity of their V muscular

mechanism due primarily to the monismostylic type of skull characteristic of these forms.

In the second group, as exemplified by *Boa*, *Varanus*, and also *Anolis* (Willard, l. c.), the motor V nucleus is for the most part ventrally or rather peripherally placed, and in relative size it is noticeably larger than the corresponding nucleus in *Alligator* and chelonians (figs. 11 and 12). In the former animals the chief bulk of the motor V nucleus lies in a position analogous to that occupied only by the caudoventral moiety in *Alligator*. In *Varanus* and *Anolis* a small portion of this nucleus still retains a relatively dorsal position, but in *Boa* this dorsal moiety has been lost.

The ventral (peripheral) position of the motor V nucleus in the above-mentioned representative of the reptilian group *Squamata* is evidently to be correlated with the increased complexity of the V jaw musculature. The degree of differentiation of the m. capiti-mandibularis in these forms, however, presents no advance over the condition obtaining in this muscle in *Alligator*; but in the development of the so-called pterygoid muscular complex a marked specialization is evident. In the development of the streptostylic form of skull the complexity of this musculature is directly proportionate to the degree of movability of the bones concerned and the pterygoid muscular complex of the *Squamata* has been acquired to meet the needs of the movable quadrate, and thus, as Adams has emphasized, must be a caenotelic character.

If, then, the peripheral position and large size of the motor V nucleus in the *Squamata* examined be correlated with the increased complexity of the V jaw musculature, it follows from the above remarks that it must be the pterygoid part of this musculature that has exerted most of this influence. The ventro-peripheral position of the V motor nucleus in these forms must also be regarded as a caenotelic character independently acquired.

As Kappers has pointed out, the most important center acting reflexly upon the motor V nucleus in reptiles appears to be that of the chief terminal nucleus of its own sensory root (31). To this general statement no further facts can be added at this time.

3. *Eye-muscle nerves*

Nerve VI. In the descriptive portion of this paper it was noted that the number of the emergent abducens rootlets and the level of their exit from the brain stem in reptiles was subject to considerable variation. Corresponding variations in the relative position of the abducens nucleus are also to be observed in reptiles, and in this respect they afford a striking contrast to the condition obtaining in this area among amphibians.

It has been pointed out that in its primitive position the abducens nucleus is dorsally placed in intimate contact with the fasciculus longitudinalis medialis and lies caudad of the exit level of the motor VII root. In this location it is found in selachians, ganoids, dipnoans and amphibians. (figs. 10 and 11).

In *Damonia* the abducens nucleus and roots retain their primitive position, but in *Chelone* the nucleus is elongated somewhat in a rostral direction and some of the VI rootlets emerge on a level with the motor VII root. A similar condition obtains in *Alligator*, but in the more recent *Squamata* (*Boa* and *Varanus*) all the abducens rootlets emerge rostrad of the motor VII and the abducens nucleus as a whole has shifted rostrad.

In reptiles the ventral tectobulbar fiber system is of but small size while the dorsal tectobulbar fibers are considerably developed (de Lange, 11). Further, the vestibular nuclei become for the first time in phylogeny considerably elaborated in reptiles (Holmes, 27). Finally, Kappers has demonstrated that a constant relationship may be observed between Deiters' nucleus and the rostral end of the abducens nucleus.

On the basis of these facts Kappers has shown that the position and morphology of the abducens nucleus in the different reptilian forms examined may be directly correlated with the rise in importance of the dorsal tectobulbar tract and vestibular system within the brain stem of these animals.³

In *Boa* and *Varanus* an abducens root and nuclear pattern obtains which resembles that constantly found in many mammals

³ For a full discussion of this subject reference should be had to Kappers' earlier papers, especially 31 and 32.

and birds, but which differs from the pattern characteristic of the more ancient reptilian forms (chelonians and crocodilians) and of amphibians. This would appear to be but another example of analogous or convergent evolution (5, p. 422).

Nerves III and IV. In respect to the relation of their oculomotor and trochlear nuclei and roots the reptiles examined are divisible into two groups, viz., those showing distinct evidence of relatively high specialization of the elements of this complex and those in which such evidence is lacking (*vide supra*). To the former group belong Alligator, Chamaeleon, Varanus, and probably Sphenodon; to the latter group belong Boa, Damonia, Chelone, and possibly Anolis.

The specialized features to which allusion is made are as follows: the apposition or close approximation of oculomotor and trochlear nuclei (i.e., the trochlear nucleus is rostrally placed); the exit of the trochlear root on a level with its nucleus; the differentiation of the oculomotor nucleus to form distinct cell groups (i.e., dorsolateral and ventromesial cell groups). All these features are in varying degrees characteristic of the animals mentioned above in the first group, but are not present among those of the second group.

The contrast between the grouping of these forms on the basis of the motor V nuclear pattern and that based on the arrangement of the elements of the oculomotor and trochlear nuclei is marked. In the former case some definite relation was apparent between the degree of specialization of the effector mechanism of the jaws and that of the motor V nucleus. In the present instance, however, with the possible exception of Chamaeleon,⁹ all the reptilian types examined exhibit a singular uniformity in the development of their extrinsic oculomotor effectors.

Among amphibians a subdivision of the oculomotor nucleus into medial and lateral moieties occurs apparently for the first time in phylogeny in *Rana* (and probably in most opisthoglossal

⁹ The eyes of chameleons are unique among reptiles in the freedom and independence of their movement, though vision in these animals as in other reptiles is monocular (Gadow, 18, p. 569).

anurans). In these forms, in contrast to gill-breathing ichthyopsidans, the eye when at rest is normally focused for distance, and it has been suggested that the development of the somewhat specialized oculomotor nucleus observed in *Rana* was probably to be correlated with the acquisition of this type of visual apparatus (5).

In most reptiles as in anurans the eye at rest is focused for distance, i.e., parallel rays are brought to focus on the retina without accommodation effort. In reptiles, with the exception of snakes, the mechanism for accommodation has become highly elaborated through the development of a striate ciliary musculature. With the foregoing exception the striate ciliary musculature is well developed in all reptiles and especially so in chelonians (Wiedersheim, 44, p. 282). By the action of this ciliary muscle on the lens capsule the curvature of the latter may be altered and accommodation effected as in mammals. In snakes the mechanism for accommodation resembles that obtaining in amphibians where the lens itself is shifted in its entirety.

The m. sphincter iridis in most reptiles is composed of striate muscle fibers, so that in general these forms, with the possible exception of snakes, may be said to possess a highly developed and complex intrinsic ocular effector mechanism.

From the above observations it might be concluded that the relatively slight differentiation of the oculomotor nucleus in *Boa* is to be correlated with the absence of the striate ciliary mechanism in this form. To some extent no doubt this may be true, but certainly no such explanation can be offered for the slight amount of oculomotor nuclear differentiation observed in *Chelone* and *Damonia*, nor does it appear that the ciliary mechanism is more highly developed in *Alligator* and *Varanus* in correspondence with the evident oculomotor nuclear specialization of those forms.

Alligator and *Chamaeleon* resemble one another and differ in degree at least from the other reptiles examined in one respect, viz., in the presence in the retina of a recognizable fovea centralis or point of maximum visual acuity (Slonaker, 45). It is highly probable that in *Varanus* a similar condition obtains. The fovea centralis is especially well developed in *Chamaeleon*, there

it constitutes a retinal area but slightly less specialized than the fovea of birds (Cajal, 9, p. 349).

Thus it would appear that the intrinsic differentiation of the oculomotor nucleus in reptiles is a reaction in response to the need for a greater nicety of muscular adjustment created by the development in the retina of a point of special visual acuity and is not to be directly correlated with the evolution of a special mechanism of accommodation.

CONCLUSION

The cerebral motor nuclear pattern in reptiles is subject to considerable variation among the members of the different orders examined. With regard to the disposition of the visceral motor nuclei, however, one feature in particular has been found in all reptiles examined to be more or less characteristically developed, viz., the common and isolated VII-IX motor nucleus. In no other vertebrate class does this nuclear association become a group character, though it has been observed to occur in such widely dissociated forms as *Lophius* and *Canis*.

It has been suggested above that the central association of the IX motor elements with those of the motor VII and the dissociation of this complex from the motor vagus column is probably to be correlated with the divorce of the glossopharyngeal effectors from primarily respiratory action. Viewed in this light the motor VII-IX nucleus of reptiles is to be considered as a center chiefly concerned in the deglutition reflex. This would be in accord with Kappers' earlier conception that the reptilian motor VII-IX nuclear association was brought about through the neurobiotaetic action of the caudally placed VII-IX taste center.

In the synapsid and diapsid forms examined the caudal end of the dorsal X motor column is prolonged into the upper segments of the cord to form the nucleus of the accessory nerve. Among the Squamata the accessory nucleus is also well developed in *Varanus*, but in *Boa* no indication of the nucleus is to be found.

Until recently it had been supposed that the absence of the accessory nerve and nucleus in *Boa* was due to changes subse-

quent to the loss of the ophidian shoulder-girdle. Since, however, among the Lacertilia, Willard has found no trace of the accessory nerve in such a form as *Anolis*, it is possible that this nerve may have been absent in the saurian type from which ophidians were derived.

The rostral extent of the hypoglossal nucleus is singularly uniform among reptiles and in its overlap of the vagus motor area presents a marked advance over the more primitive condition obtaining in amphibians. These changes in the mutual relations of the hypoglossal and motor vagus areas have been shown to be the result of an actual displacement rostrad of the former nucleus evidently under the reflex influence of the VII-IX taste center and the nucleus of termination of the ramus lingualis V which appears in phylogeny for the first time in reptiles.

A considerable range of variation is to be observed in the topographical relations of the motor V nucleus in reptiles. In *Damonia* the motor V nucleus has to a great extent retained its primitive dorsal position on the level of its root exit. In *Boa* and *Varanus*, on the other hand, the motor V nucleus is almost wholly ventral (peripheral) in its position, while in *Alligator* an intermediate condition may be recognized. The degree of ventral (peripheral) displacement of the motor V nucleus appears thus to vary directly with the complexity of the development of the V jaw musculature. In other words, the motor V nucleus is most ventrally (peripherally) placed in streptostylic reptiles and, further, it is probable that in these forms it constitutes a recent character independently acquired.

Similar examples of analogous or convergent evolution are to be observed among reptiles in the variations in the arrangement and specialization of the eye-muscle nuclei. Thus in *Boa* and *Varanus* the abducens root and nuclear pattern resembles that constantly found in many mammals and birds, but differs markedly from that obtaining among crocodilians, chelonians, and amphibians examined. Again, in the disposition of the trochlear nucleus and the intrinsic specialization of the oculo-motor nucleus, *Varanus*, *Alligator*, and *Chamaeleon* exhibit certain avian characteristics.

The dorsal position of the abducens nucleus is evidently the result of the dominating influences of the dorsal tectobulbar and vestibular fiber systems and its rostral migration in response to tecto-bulbar impulses is limited by its important reflex connections in the vestibular area (especially with Deiters' nucleus).

The rostral migration of the trochlear nucleus in response to tectobulbar stimulation in the absence of special reflex connections in the bulb is only limited by the position of the oculomotor nucleus with which in *Varanus* and *Chamaeleon* it is in close contact. It is of interest to note that the trochlear root is also displaced rostrad in these forms as in birds.

Finally, it would appear that the intrinsic elaboration of the oculomotor nucleus evident in certain reptiles has also been brought about under the influence of tectal impulses and apparently in response to the special need for precise ocular fixation due to the development in the retina of these forms of a point of maximum visual acuity.

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On the origin of the ganglion cells of the nervus terminalis of the albino rat.

Realizing that the ganglion cells of the nervus terminalis are largely of the multipolar variety, suggestive of ganglion cells of the sympathetic type, attempts have been made of late to associate them developmentally with sources known or believed to give rise to certain sympathetic ganglionic masses of the head. These sources are, briefly, 1) the trigeminus nerve and, 2) the sympathetic of the cervical region. The author had studied the proliferations from the olfactory epithelium which he believes give rise to the ganglion cells of the nervus terminalis and has searched for evidence of contributions from other sources at different periods of embryonic life. Results have been entirely negative in character, no such additional sources having been encountered.

ON THE ORIGIN OF THE GANGLION CELLS OF THE NERVUS TERMINALIS OF THE ALBINO RAT

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FIVE FIGURES (ONE PLATE)

Realizing the tendency which has existed among morphologists more recently considering the subject of the ganglion cells of the nervus terminalis to regard them as sympathetic in character, the author (Stewart, '20), in a general paper on the development of the cranial sympathetic ganglia of the rat, included a brief note on what was regarded as their probable origin. At that time it was stated that the available series was not complete in the early stages of the development of the olfactory sac and that observations were made admittedly on limited material. The conclusion attained was that the ganglion cells of the nervus terminalis apparently arose in a proliferation from the septal aspect of the olfactory sac, including the epithelium of the vomeronasal organ.

Subsequently the writer has been able to extend the series through the addition of material drawn from four litters, taken 12 days 6 hours, 12 days 6½ hours, 12 days 18 hours, and 13 days 4 hours after insemination. Nine more embryos were sectioned, making a total of sixty-eight available series.¹ The new material was fixed in the picro-aceto-platino-chlor-osmic solution of v. Rath, following the procedure of Neal ('14), it having been ascertained that the dark staining of the cytoplasm of the developing neuroblast, together with the excellent cell-

¹ The embryological series studied are part of the collection of the Department of Histology and Embryology. The writer appreciates the cooperation of Professor Kingsbury in permitting their use in the present instance. The writer likewise acknowledges the kindness of Professor Reed in criticising the manuscript.

boundary definition afforded by the method, rendered the fixer particularly desirable.

A review of the rather extensive literature on the nervus terminalis seems unnecessary, inasmuch as the presentation offered by Larsell ('18) is quite complete. Attention should be called, however, to the fact that in studies on the origin of the ganglion cells of the nervus terminalis, the older literature has been somewhat neglected. I refer to general descriptions dealing with the origin of the fila olfactoria rather than to specific papers concerned with the nervus terminalis. Disse ('97) has shown that in the bird, the fibers of the nervus olfactorius are outgrowths of typical cells of the olfactory epithelium—neuroblasts—and has noted the presence of ganglion cells appearing simultaneously among the growing fila olfactoria. Disse noted the massing of cells of the olfactory fila into an 'olfactory ganglion' and observed the similarity of cells, situated in the 'ganglion' and in the olfactory fila to those of the olfactory pit. He regarded them² neuroblasts which had wandered out from the wall of the olfactory pit. Disse figures both unipolar cells with processes directed centrally, and bipolar cells—one process directed toward the olfactory epithelium, the other passing centrally (his figs. 6, 7, and 8). The observations of Disse confirmed the earlier findings of Pogojeff ('88) and likewise had bearing on such suppositions as that of v. Lenhossék ('92) to account for the presence of free nerve terminations in the olfactory epithelium. The former observed bipolar cells among the olfactory fila of petromyzon. The interpretation of v. Lenhossék may be summed up in a brief quotation: "Es könnte sich höchstens um Nervenzellen handeln, die in den Verlauf der Olfactoriusbündel eingeschaltet sind. Hierfür sind einstweilen

² "Fassen wir den am Riechnerven gewonnenen Befund kurz zusammen, so ist nachzuweisen, dass ein kleiner Teil von Neuroblasten den Epithelbezirk, in dem er entstanden ist, verlässt, und in das anstossende Mesoderm einwandert. Soweit es sich beurteilen lässt, liegen die ausgewanderten Neuroblasten einzeln und bilden niemals Gruppen; sie zerstreuen sich über den ganzen Verlauf des Riechnerven, und treten in Verbindung mit dem centralen Ende, sowie mit dem Ursprungsbezirke dieses Nerven. . . . Die aus diesen Zellen zur Riechgrube ziehenden Nervenfasern endigen frei an der Oberfläche der Epithels."

noch keine positiven Anhaltspunkte vorhanden. Allerdings ist es möglich, dass solche in der Folge noch beigebracht werden."

Apparently Disse should be added to the list of investigators who have dealt with the origin of the ganglion cells of the nervus terminalis, and v. Lenhossék to those inferring their existence. Indeed, the work of Disse is so noted by Döllken ('09). His ('89), too, perhaps should be added to the roll. In a human embryo of four weeks His described cells resembling neuroblasts in the olfactory epithelium. With the assumption of a bipolar form these cells deserted the confines of the epithelium and in an embryo one week older they were found connected with the central nervous system on one hand and with the olfactory epithelium on the other.

From the general description given by Disse it would seem to the writer that the ganglion cells of which he treats are those which later investigators assign to the nervus terminalis, and a similar interpretation is doubtless to be placed on those studied by Pogojeff and His. A discussion of the papers of Loey, Johnston, Belogolowy, and Brookover is unnecessary. Their papers are too well known and besides have been considered but recently by Larsell. In later investigations—those of McKibben ('14), Huber and Guild ('13), and Larsell ('18, '19), it is quite universally agreed that by far the majority of the ganglion cells of the nervus terminalis are of the multipolar variety. Bipolar cells are nevertheless encountered—by Larsell ('18) in considerable numbers. In view of the predominance of multipolar cells in the ganglionic clusters of the nervus terminalis attempts have been made to derive them from sources known or supposed to furnish cell contributions to the sympathetic ganglionic masses of the head. Such a tendency is to be noted in the interpretation suggested by Hardesty ('14) that the ganglion cells of the nervus terminalis are to be thought of as belonging to the general forward growth of the trunk sympathetic into the head region—a supposition which the writer ('20) has considered scarcely tenable. It again finds expression in the more recent suggestion of Larsell ('19), that the ganglion cells of the nervus terminalis originate from two sources—one of which consists in migratory

cells occurring along the ophthalmic division of the trigeminus. The writer has attempted in the present study to follow out the proliferations from the olfactory epithelium and at the same time to seek for possible evidences of a spreading-in of cells from other sources, namely, 1) as forward extensions from the cervical region, that is, growth forward along the internal carotid nerve; 2) migrations along trigeminus branches, and, lastly, 3) elements possibly entering from the sphenopalatine ganglion.

Individuals of a litter present considerable variation, thus making it possible at one age to secure several stages. In general it may be said that the earliest proliferations from the olfactory epithelium, in the albino rat, occur between the ages 12 days 6 hours and 12 days 6½ hours after insemination. I have but one embryo of the 12-day-6-hour litter sectioned. In this embryo the olfactory epithelium is still in the plate stage. It consists in its thickest part of some seven layers of nuclei. Certain of its cells possess an elongate, spindle-shaped process directed centrally, but in no instance has the process been traced beyond the limits of the epithelium. The mesenchyme shows a marked tendency to condense beneath the epithelium and an abundant vascular network is present. Mitotic figures are numerous in the epithelium. At this stage the ramus ophthalmicus V contains large numbers of fusiform neuroblasts situated en masse from the Gasserian ganglion to the posterior border of the optic stalk. The nuclei are elongate and the technique permits the following of the processes a distance of some four or five times that of the nuclear length in either direction. The cells situated farthest out on the ramus ophthalmicus resemble in every way those on the Gasserian ganglion. A description of the early ramus ophthalmicus has been given in an earlier paper ('20) under the consideration of the ciliary ganglion.

In the earliest stage encountered in the 12-day-6½-hour litter, the olfactory plate has become transformed into an exceedingly shallow pit. Its thickened epithelium is traceable through thirty-six sections (sagittal). In this embryo the first evidence of proliferations giving rise to cells which leave the epithelium is noted. The zone of proliferation is first met with six sections

laterad of the medial edge of the depression comprising the pit, and has been followed through six sections. Evidently, then, the earliest proliferations from the olfactory epithelium are in the territory presumably of the future septal epithelium. This early outgrowth is illustrated in figure 1. The figure is taken from a photograph, slightly retouched. The olfactory epithelium, using this term to designate the general epithelium lining the olfactory sac rather than restricting it to the later highly specialized sensory epithelium, has thickened somewhat over the preceding stage, but its actual maximum number of nuclear rows is difficult to ascertain on account of the plane of section. The proliferation figured is situated amid two vascular channels and is intermingled with the condensing mesenchyme. Nevertheless, it is seen that the cells budded off from the epithelium are elongate and that one (*n*) clearly possesses a process extending peripherally into the olfactory epithelium for a considerable distance. The nuclei are elongated, ovoid, or kidney-shaped. At this stage, the ramus ophthalmicus trigemini appears no more extensive than in the former one. Certain of its spindle-shaped cells show a tendency to round out and their cytoplasm is acquiring the darkly staining characteristic of the neuroblast. The ophthalmicus does not approach the zone of proliferation from the olfactory epithelium, nor does the maxillaris. Contributions from other of the above-mentioned possible sources are even more absolutely excluded at this time. The relation of the spindle-shaped cell (*n*), should no further migration occur, is suggestive of the relations of the ganglion cells in the sub-epithelial plexuses, in the so-called terminal and septal territories of Ayers ('19).

In another embryo of the same litter, the process has gone much further. The olfactory pit is present on one side as a deep depression and on the other a contact is just in process of establishment with the oral epithelium, forming thereby a bucconasal membrane. Evidences of proliferation from the epithelial lining of the pit are abundant (fig. 2) and the result has been the piling up of a mass of cells in a ganglion-like aggregate (*g*). The shape of the aggregate is somewhat that of a disc, conform-

ing to the general contour of the adjacent part of the olfactory sac. The proliferation again is confined to the medial aspect of the sac. In the ganglion-like aggregate, numerous cells are distinguishable with darkly staining cytoplasm. They are too closely packed to enable one to follow processes very distinctly. In general, the nuclei appear more rounded than those just freed from the confines of the olfactory epithelium. It would seem to be this structure which Döllken ('09) has termed the ganglion terminale. That this recognition by Döllken is scarcely accurate is noted by Johnston ('13). The subsequent fate of the cells of this aggregate will be traced in later stages.

Figure 3 gives some idea of the relation of the two trigeminal strands—ophthalmicus (*o*) and maxillaris (*m*)—to the olfactory epithelium. In a fortunate section each was photographed at the point where it most nearly approached the epithelium. The maxillaris appears more extensive in the photograph than it actually is, since its foremost tip extends into elongated mesenchymal cells surrounding a vascular channel. Its anterior limit is marked by an (*x*). Although a pyridine-silver preparation might possibly show fibers extending beyond this point, the extent of migrating cell elements is believed accurately depicted in the photograph. So far, then, the proliferation from the epithelium of the olfactory sac is independent of any contribution of trigeminal origin.

Following stages (12 days 18 hours) do not show sufficient advancement to merit separate description. The mass of cells—'olfactory ganglion'—is merely increased in size. It occupies the posterior part of the septal territory, being quite closely molded to the olfactory sac. Vom Rath material does not show as yet any olfactory fila entering the brain at this stage, although they approach it quite closely.

Disregarding thirteen-day stages and passing to the consideration of embryos of the 13-day-4-hour litter, of which three are available, the following facts may be noted: The olfactory epithelium is in contact posteriorly with the oral epithelium in a bucco-nasal membrane—exceedingly thin, but as yet unruptured. The fibrous strands originating from the olfactory epithelium,

to which the general term 'fila' may perhaps be best applied, are greatly increased in number. The central growth of the fila has carried the cell bodies situated among them centrally, thus somewhat displacing the olfactory ganglion. This, coupled with the enlargement of the forebrain, tends to mold the ganglion-like aggregate to the forebrain contour. Certain few cells of the aggregate show a marked rounding-out of nuclei and a distinct cytoplasmic ring quite characteristic of a neuroblast. Others are undoubtedly destined to become sheath cells. Many seem indifferent. The author consequently would admit the partial correctness of Döllken's designation of the 'olfactory ganglion' of older writers as ganglion terminale. Reference to the figures of Disse showing early stages in the development of the olfactory fila would seem to indicate quite clearly the presence of neuroblasts in the midst of the fila—neuroblasts which undoubtedly would tend to intermingle with sheath cells and join with them in the formation of the so-called olfactory ganglion. It may be noted that certain fila at this stage arise from a portion of the epithelium which may be definitely marked out as vomeronasal.

I have been unable to trace cell-bearing ophthalmicus strands into territory where their addition of elements to the neuroblasts situated among the fila would seem possible. The same obtains for what would seem a vastly more probable source of addition, namely, the facialis. At this period the grouping of cells which marks out the site of the future sphenopalatine ganglion is clearly evident. From it cellular strands have been traced to the most posterior part of the olfactory sac in the vicinity of Hochstetter's membrane. These strands, however (and they have likewise been followed in a pyridine-silver preparation of an embryo two hours older), do not approach the cell aggregates accompanying the fila; they have not been observed to enter the epithelium. It would appear to the writer that an addition of ganglion cells to nasal territory, especially of any whose processes were related to vessels and glands, would be most probable from this direction. The facialis nerve is accompanied by elongated cells which the author has had reason to believe give

rise to the sphenopalatine ganglion. The latter ganglion receives supposedly preganglionic fibers of the facialis and distributes postganglionic fibers to the nasal cavity. One would seem justified in assuming that additions to the ganglion cells of the nasal cavity, should such additions exist, would be essentially continuations of the same migration which had originally involved the formation of the sphenopalatine ganglion. It has been shown by the author that such is the case, for instance, in the tongue, where continuation of the migration which gives rise to the submaxillary ganglion results in the formation of certain small lingual ganglia in the anterior portion of the tongue.

Passing to later embryos, however, fourteen and fourteen and one-half day stages, it has proved impossible to trace cells from the sphenopalatine ganglion, at that age very diffuse, into nasal territory, although the ganglion approaches anteriorly very close to the posterior portion of the olfactory sac. Neither has the study of trigeminus branches been productive of results. The next half-day shows little appreciable change. There is some slight evidence of a spreading forward of cells from the sphenopalatine ganglion toward the hard-palate region beneath the nasal passages. Later embryos have failed to confirm this migration. It in no way might involve intermingling with ganglion cells amid the olfactory fila. There would seem to be no way of checking Hardesty's supposition as to the origin of the ganglion cells of the nervus terminalis. I have followed them forward along the internal carotid nerve and along the great deep petrosal nerve. After the junction of the latter with the great superficial petrosal to form the Vidian, it has proved impossible to distinguish them. In view of a failure to observe a migration of cells of the sphenopalatine ganglion into nasal territory, it would seem that the other possibility, that suggested by Hardesty, is at least in part eliminated.

Embryos of the fourteen and one-half and fifteen-day litters show marked additions in cells clearly neuroblastic, especially among strands issuing from the vomeronasal organ. It may be of value perhaps to compare at this stage cells of the sphenopalatine ganglion with those situated among the olfactory fila and in the

so-called olfactory ganglion. The two regions are shown in figures 4 and 5—photographs of the same embryo, age $15\frac{3}{4}$ days, v. Rath technique, and under the same magnification ($\times 780$). The cells of the olfactory region—those clearly neuroblastic in nature—are in general rounded, with rounded or slightly oval nuclei; their cytoplasm is relatively abundant. Those in the 'olfactory ganglion' are situated mainly on its medial aspect and are traceable caudad along the bulb, along what are clearly nervus terminalis strands. The cells of the sphenopalatine ganglion still tend to lie in strand-like aggregates; they are more elongated with nuclei generally markedly oval and with rather scanty cytoplasm. The two varieties are readily distinguishable.

In brief, the process has been followed up to and including seventeen-day embryos, and no evidence of an origin, other than that earliest observed from the olfactory epithelium and continuing into fairly late embryonic life from the same source, has been obtained for the ganglion cells of the nervus terminalis. I have likewise given some attention to the suggestion of Larsell ('19) of an origin from the neural tube, and must confess similar negative results. The growth appears to me to take quite the opposite direction, no contact of ganglion cells with the brain wall occurring until late stages, when cells are carried backward with the growing nerve rootlets. To be sure, this study does not carry the problem into postembryonic or even into the really late stages of fetal life, but evidence obtained from cell counts indicates a decrease rather than an increase in those cells regarded as neuroblasts, this being in essential agreement with the observations of Huber, and doubtless likewise subject to the same sources of error. In view of this apparent decrease it would be rather difficult to assume late additions to the ganglionic aggregates of the nervus terminalis. The writer sees therefore no reason for reversing his earlier decision or the decision reached by certain previous investigators and must consider the derivation of ganglion cells of the nervus terminalis from sources other than the epithelium of the olfactory sac, i.e., from those sources suggested as possible earlier in this paper, as resting upon evidence as yet purely gratuitous.

SUMMARY

Realizing that the ganglion cells of the nervus terminalis are largely of the multipolar variety, suggestive of ganglion cells of the sympathetic type, attempts have been made of late to associate them developmentally with sources known or believed to give rise to certain sympathetic ganglionic masses of the head. These sources are briefly, 1) the trigeminus nerve and, 2) the sympathetic of the cervical region. The author has studied the proliferations from the olfactory epithelium which he believes give rise to the ganglion cells of the nervus terminalis, and has searched for evidence of contributions from other sources at different periods of embryonic life. Results have been entirely negative in character, no such additional sources having been encountered.

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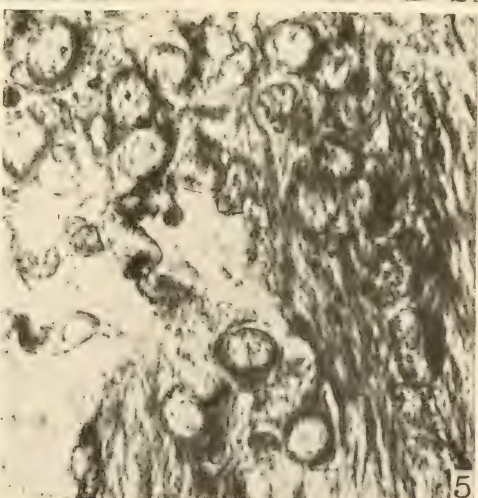
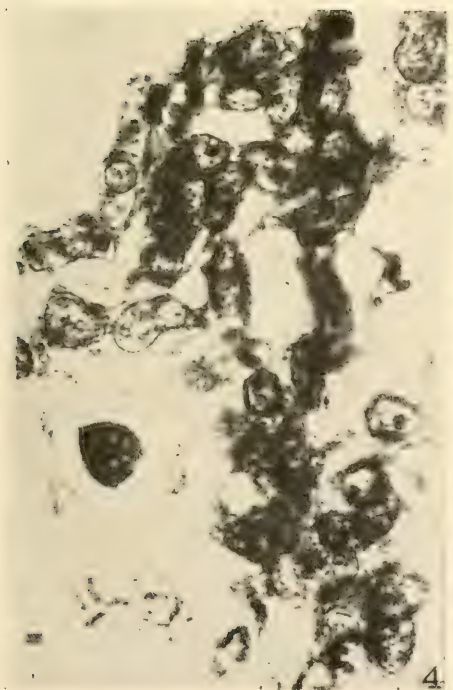
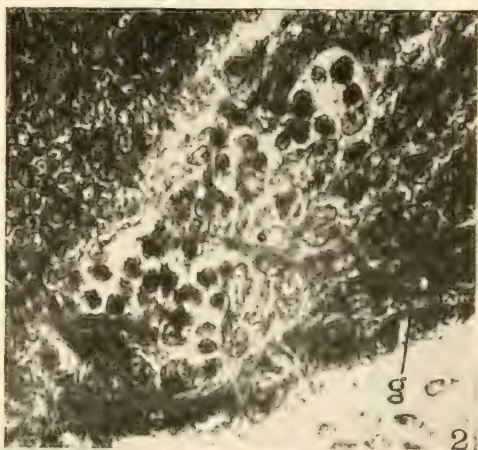
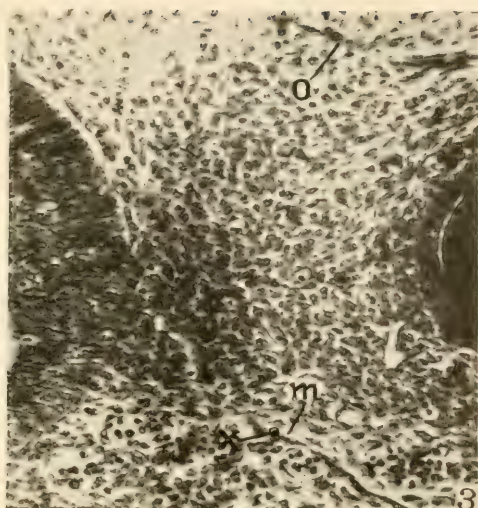
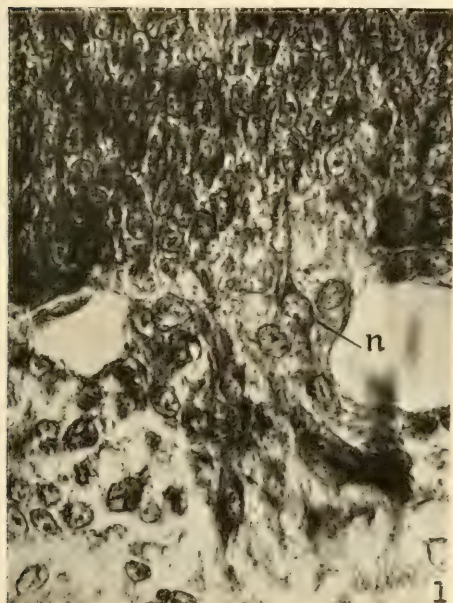
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PLATE 1

EXPLANATION OF FIGURES

- 1 Early proliferation from the olfactory epithelium. Albino rat embryo, age 12 days $6\frac{1}{2}$ hours; v. Rath technique; retouched photo. $\times 550$.
- 2 More extensive proliferation in embryo of same litter. v. Rath. technique; photo. $\times 480$.
- 3 Early ramus ophthalmicus; (*o*) and ramus maxillaris (*m*). Same litter and same technique; photo. $\times 150$.
- 4 Cells of the sphenopalatine ganglion. Albino rat embryo, age $15\frac{3}{4}$ days; v. Rath. technique; photo. $\times 780$.
- 5 Cells among olfactory fila of same embryo; photo. $\times 780$.



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The extent of the floor-plate of *His* and its significance.

The summary of this paper is as follows: 1. A differentiated floor-plate extends no farther cephalad than the fovea isthmi. Increased morphologic significance is believed to attach to this depression. 2. The plan of arrangement of the longitudinal zones of *His* as set forth by him and generally accepted is interpreted as giving a wrong morphologic basis for the brain. 3. Theoretic considerations based partly on the 'blastopore theory' indicate: a) that the floor-plate corresponds to a 'sutura neurochordalis' (*His*); b) that the floor-plate and notochordal plate are primarily coextensive; c) that the neurochordal suture does not extend to the anterior end of the neural plate; d) that the primary motor and sensory zones are continuous from side to side cephalad of the anterior end of the floor-plate. 4. The following interpretations are accepted: a) that the optic chiasma marks the anterior end of the neural plate; b) that the motor zone terminates with the midbrain; c) that the floor-plate terminates at the fovea isthmi; d) that the boundary between motor and sensory zones terminates near the mammillary recess. 5. A rational basis for the division of the brain into epichordal and prechordal portions is afforded by the interpretation presented. 6. A number of facts of cephalic and encephalic morphology may be better interpreted on the basis suggested in this paper.

THE EXTENT OF THE FLOOR-PLATE OF HIS AND ITS SIGNIFICANCE

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ELEVEN FIGURES

In 1888 Wilhelm His first set forth his well-known interpretation that the neural tube consists of four fundamental longitudinal laminae, plates, or zones—the floor-plate, the roof-plate, and the lateral plates, the last being divisible into the primary sensory zone, dorsal or alar plate, and the ventral, primary motor zone (basal plate), these being demarcated from each other upon the internal (ependymal) surface by a furrow, the sulcus limitans. In the papers by him that appeared in 1892 upon the general morphology of the brain and the divisions of the brain, and in 1893 on the frontal end of the brain tube, His further applied this conception to the brain.

The importance and fundamental character of the analysis of the neural tube in terms of primary longitudinal zones has been generally recognized, as is evidenced from the fact that in nearly every text-book having occasion to present the development of the brain and spinal cord the description is largely based upon the work of His and his figures are reproduced, among them one or more in illustration of the longitudinal zones.

The dorsal and ventral laminae composing the lateral walls of the neural tube are the zones which by their growth furnish the nervous tissue (neurones) of the brain and spinal cord, while the roof-plate and floor-plate are generally interpreted as primarily 'non-nervous,' composed of indifferent (ependymal) cells alone, although this has been frequently tacitly assumed rather than positively stated. Attention has thus been directed rather to the lateral laminae than to the dorsal and ventral medial zones that join them, which have been accordingly rather neglected.

This last statement applies particularly to the floor-plate. The roof-plate, due to the general interpretation that the choroid telas and plexuses express in each instance expansions of it, has received more consideration. Although little attention has been devoted to the floor-plate, the writer believes that the structure, extent, and significance of this portion of the developing brain and spinal cord are matters of marked importance in understanding the fundamental morphological plan of the brain, and it is the purpose of the present paper to emphasize particularly the theoretical significance of this structurally insignificant portion of the neural tube.

Descriptions of its structure are scanty, although its structural appearance is well known to every one working with the vertebrate embryo. The portion of the neural tube that it represents is apparently devoid of neuroblasts, consisting of neuroglial elements alone, which as an ependymal plate are often conspicuously evident. Processes of these cells and subsequently neuroglial fibers extend to the surface of the neural tube. It possesses thus purely negative characters for one interested primarily in the neuronal composition of the nervous system. Streeter ('11)¹ describes it concisely, as also does Strong ('16).² It is indeed this differentiation of the lateral wall referred to by Streeter and

¹ (P. 6.) "In the region of the anterior median fissure of the cord and the median raphe of the hindbrain, corresponding to the Boden-platte of His, the neuroglia maintains its primitive ependymal type of simple radial fibers extending from the lumen to the surface of the tube. It is this region that is traversed by the fibers of the anterior white commissure of the cord and the transverse arcuate fibers of the hindbrain. The persistence of this simple type of neuroglia may be explained by the absence of any mantle or nuclear layer with its consequent complications at this place."

(P. 7.) "Thus in the adult we find that the ependymal neuroglia is persistent only as septa in the anterior and posterior median planes of the nervous system and as a lining membrane for its central canal and ventricles."

² (P. 453.) "Two points are to be noted: First, that the neural plate is a bilateral structure and the future development of the tube will naturally take place principally in the side walls or lateral plates of the formed tube; second, that the primary connection between the two side walls is the ventral median plate, the dorsal median plate having been produced by a secondary fusion. This being the case, the ventral connection between the two lateral plates will naturally be more extensive and possibly more primitive than the dorsal."

which is lacking in the floor- and roof-plates that sets off both these dorsal and ventral medial zones.

The roof-plate and the floor-plate are comparable structures and this should be borne in mind in the interpretation of the latter. The roof-plate arises from the fusion of the edges of the neural plate when it forms the neural tube. It is thus primarily a bilateral structure, the two halves from the method of its formation united in an ideal dorsal line of concrescence. While in the spinal cord, medulla oblongata, and roof of the third ventricle, it differentiates as non-nervous material—dorsal septum and epithelial tela—in the cerebellum and roof of the midbrain it is so speedily obliterated that it is difficult to say that it exists at any time as a differentiated structure—a septum of non-nervous (neuroglial) elements uniting two primarily nervous plates. This would in no way affect the originally bilateral value of the cerebellum and tectum mesencephali. The same considerations apply to the floor-plate. Theoretical considerations to be discussed subsequently indicate that the floor-plate, like the roof-plate, has its two halves united by an ideal plane. In early stages of the neural tube, it is impossible to determine how much of the floor of the neural tube is non-nervous (ependymal). It is only through the growth and differentiation of the neural tube that the floor-plate becomes clearly demarcated and attains the characteristic structural features above referred to. It is quite possible that it is primarily quite slight. Throughout the extent of the spinal cord and medulla oblongata it remains relatively or completely free from nerve cells, although in certain regions (e.g., as in the pons) what appear as medial migrations of neuroblasts may quite completely transform it.

The histologic structure of the floor-plate and its significance in separating the right and left halves of the spinal cord (as the neuroglial basis of the anterior commissure) and (as the septum medullae) the caudal portion of the brain stem require no additional description or discussion. It is only when the question is raised as to how far forward into the cranial portion of the neural tube it may be traced that we reach questions touching intimately the morphology of the vertebrate central nervous system.

It was clearly the interpretation of His that the floor-plate extended throughout the neural tube and terminated at the 'anterior neuropore' where upon the completion of the closure of the neural tube it was continuous with the comparable structure in the roof. His nowhere, however, as far as I can ascertain, devotes to the question any discussion or gives any full statement. Later descriptions of the development of the neural tube, e.g., particularly the excellent descriptions of Streeter ('11), conform to this interpretation. Thus in the midbrain the existence of a floor-plate is rather tacitly assumed, as requiring indeed no comment, while in the diencephalon the floor-plate is described. If the histologic characteristics of the differentiated floor-plate as they are known in the region of the spinal cord and rhombencephalon are taken into consideration in our conception of a floor-plate, it becomes apparent that the floor-plate has a much more limited extent than is at present the interpretation. In other words, if we define the floor-plate as the medial ventral portion of the neural tube, consisting of neuroglia (ependyma) alone, devoid of neuroblasts and furnishing therefore no neuronal elements, but separating the nervous system (neural plate) into two primary right and left halves, a floor-plate is lacking, as such, in the mesencephalon and diencephalon. The floor-plate would then be recognized as extending throughout the spinal portion of the neural tube and the rhombencephalon, up to a structural feature of considerable morphologic significance, the fovea isthmi, and there rather abruptly terminating. Cephalad of this point, that is, in the floor of the midbrain, we find, not ependyma alone, but differentiation in terms of ependymal, marginal, and mantle zones, such as is encountered in the lateral walls of the neural tube.

The fovea isthmi, to which attention is drawn when seeking the anterior end of the floor-plate, requires brief notice in passing. It was first described by Stieda ('75), Burekhardt ('91) and myself ('95) in the amphibian brain. At that time I referred to it as the mesencephalic pit. His had previously termed it in the embryo the 'Isthmusgrube' ('92, 1), and indicated its presence in frog, shark, salamander, trout, sturgeon, chick, and man.

Corresponding to the medial depression internally, His described a prominence externally to which he gave the name of *eminentia interpeduncularis*. Herrick ('17) has recently reexamined the fovea isthmi in the amphibian brain. It may conveniently be regarded as marking the caudal boundary of the midbrain on the medial floor. Herrick uses the term fovea isthmi, which is here adopted. Von Kupffer ('06) terms it the '*sulcus intraencephalicus posterior*.' He figures it in all classes of vertebrates save the elyostomata and the Mammalia (the latter class was not included in the limits of his presentation). Johnston ('09), who figured the medial plane in the brains of shark, salamander, and mammal, shows the fovea isthmi only in the salamander. In the medial plane reconstructions of the developing brain of shark, bird, and mammal, reproduced here as figures 1, 2, and 3, it is evident in all. The floor of the midbrain anterior to the fovea isthmi is without adequate embryological designation. For the German terms Haube, Haubenwulst as applied to the mesencephalic floor, 'tegmental swelling,' 'tori tegmentales,' and 'tori semicirculares' have been used. The '*tuberculum posterius*' of von Kupffer may be taken as marking the anterior boundary of the mesencephalic floor.

To illustrate the abrupt termination of the differentiated floor-plate at the fovea isthmi, three reconstructions were made of the midsagittal plane, from three classes of vertebrates, the elasmobranch (*Acanthias*), the bird (chick), and the mammal (calf). These are reproduced as figures 1, 2, and 3. It will be seen that the differentiated floor-plate, characterized by the presence of the ependymal layer only and the neuroglial processes (neuroglia fibers), often grouped together in parallel radial bundles, terminates at the fovea isthmi and cephalad of this point, in the floor of the midbrain, the characteristic arrangement of the floor-plate is lacking, while ependymal, mantle, and marginal layers appear. In other words, the differentiation shown is that characteristic of the lateral wall of the neural tube. Cephalad of the midbrain the medial floor thins in the hypothalamic region, to thicken again at the chiasma. Inasmuch as the low magnification for these medial plane reconstructions necessitated

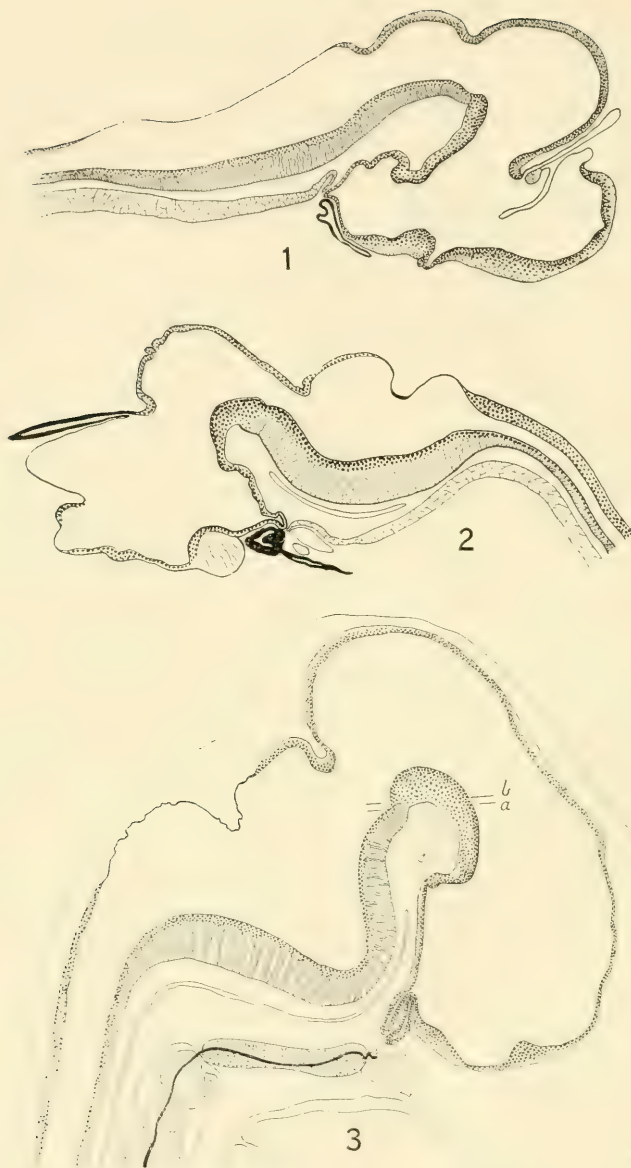


Fig. 1 Reconstruction of the middle plane of the brain, together with notochord and hypophysis in *Squalus acanthias* embryo, 40 mm. total length. $\times 10$.

Fig. 2 Medial plane reconstruction of the brain, notochord, and hypophysis in a chick of seven and one-half days' incubation. $\times 10$.

Fig. 3 Medial plane reconstruction of the brain, hypophysis, notochord and basilar plate in a calf embryo of 23 mm. length. (Series C.25, Cornell University Collection.) $\times 10$.

In these figures the floor-plate is indicated by the parallel, somewhat irregular lines representing the fibers of the floor-plate.

that the representation of the structure be quite diagrammatic, photographs from the sections showing the median plane at the fovea isthmi are reproduced as figures 7, 8, and 9. Of these, that of the calf embryo shows the median plane throughout, while in figures 8 and 9 only the extent indicated is medial. In figure 9, the pulling away of the neural tube from the mesenchyme has accentuated the 'eminencia,' making it more abrupt, while the outline of the external surface cephalad of it is poorly defined. It will be seen, particularly in the reproductions from the calf and shark embryos (figs. 7 and 8), that the statements made above are fully confirmed by the photographs.

Two additional photographs from frontal sections of a calf embryo (20 mm.), through the summit of the mesenchyme in the plica encephali ventralis³ and somewhat more dorsally are given for comparison (figs. 10 and 11). The general position of these levels is indicated upon the medial plane reconstruction (fig. 3) by the lines 'a' and 'b.' It may be noted that in figure 10 the floor-plate is shown in the caudal limb of the bend and its absence in the cephalic (mesencephalic) limb or portion. The more dorsal section (fig. 11) is through the cephalic end of the floor-plate where the letter 'c' indicates its limit.

The question of the significance attaching to the termination of the floor-plate anteriorly at the fovea isthmi involves the interpretation of the cephalic portion of the neural tube, and brings up for consideration the much-discussed question of the anterior end of the neural plate and of the neural tube itself. The conclusions reached by His were given in 1888 and particularly in 1892 in his paper on the general morphology of the brain. They are well illustrated by his figure 1 from the latter article, which is reproduced here as figure 4. The anterior end of the floor of the neural tube he placed at the 'Basilarleiste' 'B' (basilar fold) later to become, according to his interpretation, the recessus infundibuli. The dorsal wall of the tube, due to its great curva-

³ This term introduced by v. Kupffer and meaning, as its composition implies, 'ventral brain fold,' seems to the writer more useful in this connection than 'cephalic flexure' ('head fold') for which it is a partial equivalent.

ture, is more extensive. The floor-plate thus terminates at the basilar fold (*recessus infundibuli*); the roof-plate marks the extent of the medial dorsal wall; while a line of closure at the anterior end of the tube, in the territory of the future *lamina terminalis*, obliterates the anterior neuropore. "All three medial plates of the brain tube correspond to original seams of closure,"—a dorsal seam (*dorsale Naht*), a ventral or neurochordal seam (*neurochordale Naht*) and an anterior or frontal end-seam (*frontale Naht*).⁴ The *sulcus limitans*, bounding the basal plate from the alar plate, he considered as terminating at the optic recess (i.e., preoptic recess). His conception of the brain tube is thus clear: that in the neural tube there was a dorsal line of closure and an anterior (frontal) line of closure, while the neural plate itself was completely separated into two halves by a floor-plate which itself represents a line of closure in the laying down of the body, by concrescence, hence the term '*neurochordale Naht*' which he used.⁵

The brain-plate was thus interpreted as a completely paired structure, consisting of two separate halves united through con-

⁴ His offered no technical designations for these seams of closure which he recognized. These were supplied by Goronowitsch ('93), who termed them '*Sutura neurochordalis seu ventralis*, *Sutura terminalis anterior*, and (by implication) *Sutura dorsalis*. He failed, however, clearly to appreciate what His meant by '*Neurochordale Naht*.' His words are (p. 203): "*Von der vorderen Grenze der Leisten (gl) verläuft ein Spalt (f), welcher ventralwärts bis zu der Gegend a reicht, wo die ventrale Hirnwand mit den unterliegenden Theilen in Verbindung steht. Diesen Spalt welche ich einfach Sutura cereбрalis anterior bezeichne, da ich eine Zersplitterung dieses Terminus in zwei Termini "Sutura neurochordalis, seu ventralis und Sutura terminalis anterior (His) für meine Zwecke überflüssig finde (vergl. 32, pag. 7)."*

⁵ His ('92, 2), (p. 348): "*Alle drei Säume des Medullarrohres entsprechen ursprüngliche Nahtlinien. Am längsten ist die dorsale Naht (d.N.) bekannt. Die ventrale oder neurochordale Naht ist zur Zeit noch von Manchen Seiten her bestritten. . . . Ungenügend gewürdigt ist auch die vordere oder frontale Endnaht (f.N., Fig. 1). Sie entsteht durch Verbindung der vorderen Ränder der Medullarplatte und nimmt bei allen Wirbelthieren eine durchaus selbständige und charakterische Stellung ein. . . . Die Wand des Medullarrohres ist in den an die Nahtlinien anstossenden Strecken in Allgemeinen dünner, als in den beiden Seitenwänden, die verdünnte Strecke der ventralen Röhrenwand ist die sogenannte Bodenplatte, die der dorsalen die Deckplatte. Die verdünnten Nahtstrecken der vorderen Naht liegen im Boden des dritten Ventrikels und in der Lamina terminalis."*

crecence and joined together by the floor-plate. I shall recur to this later. His figure 8, from his ('93,1) paper on the frontal end of the brain tube, reproduced here as figure 5, illustrates this clearly. Johnston ('09), from a study of the early developmental stages in the shark, the salamander, and the pig, has given valid

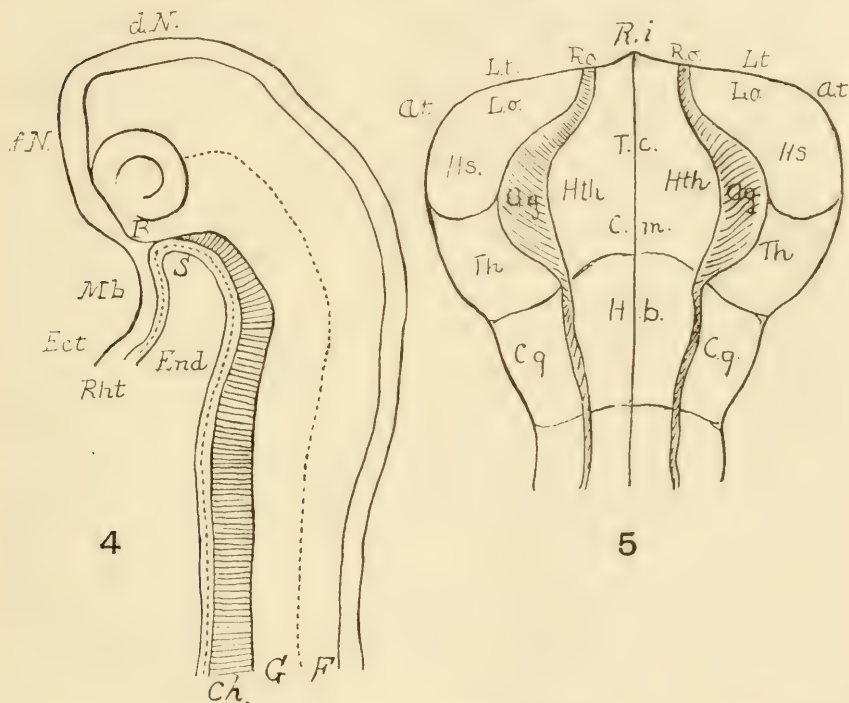


Fig. 4 Copy of figure 1 of Wilhelm His ('92, 2). Schema in explanation of the bent brain tube and its relations to chorda dorsalis (*Ch.*), to Sessel's pocket (*S*) and to the pharyngeal membrane (*Rht.*). *d.N.*, dorsal seam (*Naht*); *f.N.*, frontal seam; *Mb.*, stomodeum; *G.*, basal plate; *F.*, alar plate; *B.*, basilar fold (*Basilarleiste*).

Fig. 5 Copy of figure 8 of Wilhelm His ('93, 1). The attempt is made to project the individual brain regions upon the medullary plate of a selachian at a stage in which it is still spread out flat. The regions are indicated as follows: *Ag.*, optic vesicle; *At.*, angulus terminalis; *C.m.*, corpus mamillare; *C.q.*, corpus quadrigeminum; *Hb.*, tori tegmentales (*Haubenwülste*); *Hs.*, pallium cerebri; *Hth.*, hypothalamus; *Lo.*, lobus olfactorius; *L.t.*, lamina terminalis; *R.i.*, recessus infundibuli; *R.o.*, recessus opticus; *T.c.*, tuber cinereum. The region of the optic chiasma would be between *R.i.* and *R.o.*

evidence that the rostral (cephalic) end of the neural plate in the closed neural tube is marked by the anterior boundary of the optic chiasma, that is, is located at the preoptic recess. His termed this recess the optic recess as marking on the middle plane the level of the optic evaginations. Johnston points out that the preoptic recess is secondary and that the basilar furrow of His (Basilarleiste), which he regarded as becoming the recessus infundibuli, in reality marks the level of the optic evaginations. Johnston therefore calls the basilar furrow of His the primitive optic furrow, which he concludes may persist as a postoptic recess. These points of disagreement with the conclusions of His do not particularly concern us here, aside from his conclusion that the anterior end of the neural plate includes the optic chiasma. The experimental results of W. H. Lewis ('12), Spemann ('01) and Stockard ('13), indicating as they do that the anterior end of the neural plate is occupied by the retinal area (or areas), would in a general way confirm this. Johnston further says (p. 462) that "The determination of the anterior end of the brain will fix the extent of the floor-plate and roof-plate of His and will show the point at which the prolongation of the sulcus limitans must end;" and further concludes (p. 504) that "The optic chiasma therefore occupies the anterior border of the floor-plate of the brain." Johnston thus extends the floor-plate farther forward than did His, and apparently, like His, regarded it as completely dividing the cranial portion of the neural plate into two halves. His wording in regard to this is not entirely clear, as appears from the above quotation.

Schulte and Tilney ('15), in a study of the morphogenesis of the neuraxis and the interpretation of the forebrain in terms of the longitudinal zones of the neural tube, have likewise dealt with the problem involved. Their conclusions are based upon the conditions in twenty-six young cat embryos cut in the transverse plane as studied in wax-model reconstructions. They find that the anterior end of the neural plate is marked by a swelling, the 'tubercle of the floor,' which is located at the anterior extremity of the floor-plate. This tubercle, according to their interpretation, becomes the mammillary region. The medial plane of

the floor of the brain cephalad of this point would thus represent a secondary concrescence of the edge of the neural plate. In other words, in terms of the His nomenclature, they would extend the frontal suture caudally in the floor so as to include in its territory not only the optic chiasma (as did His), but the infundibulum as well. Their interpretation thus departs widely from that of Johnston. They approach his interpretation, however, in deriving the infundibular recess from the primitive optic vesicles.⁶

No comment need be made on the interesting conclusions of Schulte and Tilney save to emphasize that the critical point is the interpretation of the 'tubercle of the floor' and to venture the opinion that the figures offered in illustration neither conclusively show that it corresponds to the anterior end of the neural plate nor that it marks the anterior boundary of the mammillary recess. The floor plate, as such, and the question of its extent, they do not specifically discuss.

As is of course well known, His had in a number of articles ('76, '77, '77, '91) proposed and supported the view that the axis of the vertebrate body was established by the concrescence of a 'germ ring.' His last discussion of concrescence ('91) was a paper read at the meeting of the Anatomische Gesellschaft, and in the discussion his conception of concrescence met with considerable adverse criticism. He therefore welcomed the support O. Hertwig ('92) gave to the theory of concrescence through the publication the next year of his classical paper, "Urmund und Spina bifida." Hertwig's conclusion, however, that the 'neurochordal seam' was laid down by the concrescence of the right and left halves of the (dorsal) blastoporic lip, he could not accept.

⁶ Schulte and Tilney ('15), (p. 340): "As the tubercle of the floor constitutes the extremity of the floor-plate and at the same time the primitive ventral lip of the neuropore, it is of prime importance to ascertain its position in subsequent stages of development." (P. 341.) "The tubercle of the floor is now losing its demarcation from the parietes with the effacement of the primitive ventral segment of the optic sulcus, and from this period appears as a transverse ridge intervening between the mammillary and infundibular regions. It is, therefore, evident that the mammillary region arises from the cephalic extremity of the primitive floor-plate and that the infundibular region is a derivative of the primitive optic vesicles."

This failure to appreciate the importance of Hertwig's 'blastopore theory' for his own 'conrescence theory' seems to lie mainly in his inability to see how the primitive streak could in any way correspond to a blastoporic lip. Minot ('90, '92), on the other hand, who was an energetic champion of the theory of conrescence, clearly recognized—independently of Hertwig's experimental evidence—that "conrescence is a method of uniting the lips of a greatly elongated gastrula mouth." Since the year 1892 investigations upon the early development of the vertebrate body have contributed fact and interpretation both for and against conrescence. The blastopore theory, however, gives us the more fundamental conception. From the dorsal lip of the blastopore, or the primitive streak that clearly represents it essentially, is formed by differential growth in that region, neural plate, notochord, mesoderm. For this the evidence aside from that experimental and teratological, though largely indirect, is cumulative and conclusive. The growth of the blastoporic lip (primitive streak) essentially constitutes a closure of a primitive blastoporic opening by means of a conrescence, actual or potential. The conrescence theory thus loses all force or application aside from the blastopore theory. The sutura neurochordalis only has significance as a line of conrescent closure if it is conceived as formed along the line of growth of the dorsal blastoporic lip.

It seems a little remarkable that His, entertaining as he did the view that the body axis is laid down by conrescence of a germ ring, should have failed to recognize that there was a high probability at least that anteriorly to the line of conrescence the body material should be primarily continuous and that the neurochordal suture could not extend fully to the secondary line of closure—the frontal suture closing the neural tube anteriorly. Indeed, in his 1891 paper on conrescence, here and there, particularly in his discussion of the formation of the embryo from the primitive streak (p. 76), as well as in his figures, are indications of his recognition of a 'preaxial' portion of the body, but he never apparently saw the import of this for his own theory. Minot ('92) in this respect clearly appreciated that there is a primitive

continuity cephalad of the line of concrescence (closure), as his figures (figs. 64, 66, 67, and 74) show. In terms of the blastopore theory, it is evident that at the anterior end of the line of closure there would be continuity of the blastoporic lip of either side, and that the lateral plates of the neural plate would be continuous across from side to side at this point. Although he did not attempt to determine in what portion of the brain-plate and brain tube such a primary continuity across from side to side cephalad of the neurochordal suture would reside, Hertwig ('92) leaves no doubt of his full recognition of the necessary occurrence of such continuity at this point as an essential part of his interpretation.⁷

His, with his customary acumen, recognized that "it is just in the earliest stages that the key to the understanding of all later manifold complexities in the conformation of the brain must be sought;" that the fundamental plan of arrangement of the brain tube may be mapped out in the neural plate. This he attempted to do ('93, 1) in his figure 8, which has been already referred to and copied in this article as figure 5. The attempt was clearly premature, as the work of Johnston ('09) and others have shown. It is still of course premature to offer a diagram

⁷ Hertwig, O. ('92), (pp. 372-373): "Wir erhalten auf diese Weise eine Gastrula-form bei welcher der noch weit offene Urmund, der vom Kopfe nach dem Schwanzende zu etwas in die Länge gezogen ist, ringsum von der Anlage des Nervensystems eingeschlossen ist. Die Urmundränder selbst bilden eine etwas gekrümmte, nach aussen frei liegende Nervenplatte, einen Medullarring. . . . Das periphere Nervensystem zerlegt sich so ganz naturgemäss nach seiner örtlichen Entstehung in einen sensiblen, von dem äusseren Rande des Nervenrings, und in einen motorischen, von seinem inneren Rand ausgehenden Abschnitt. Indem auch bei den Wirbelthieren das Centralnervensystem, wie unsere Missbildungen so deutlich zeigen, als Ring in der Umgebung des Urmunds zur Anlage kommt, bietet sich eine sehr einfache, von mir (Lehrbuch d. Entw. ges.) schon früher kurz dargelegte, morphologische Erklärung für den Bell'schen Lehrsatz oder die Thatsache des getrennten Ursprungs der sensiblen und motorischen Wurzelfasern." . . . (Pp. 373-374.) "Die Beziehung des Centralnervensystems der Wirbelthiere zum Urmund (Primitivrinne, Blastoporus) sind schon oft erörtert und anerkannt worden. Dabei ist ein Punkt im Unklaren geblieben, die Ausdehnung nämlich, in welcher der Urmund des Centralnervensystem seiner Länge nach gespalten hat. Durch die vorliegende Hemmungsmissbildung ist auch in diese Frage mehr Klarheit gebracht. Die Urmundspalte hat ursprünglich das ganze Centralnervensystem in zwei gleiche, an ihren Enden zu einem Ring geschlossene Hälften zerlegt." Also compare pages 424-452.

alternative to that of His. However, inasmuch as I have in this paper attempted to show that from the actual facts of structure the floor-plate extends no farther forward than the fovea isthmi, and that theoretic considerations strongly speak against its extending to the extreme anterior end of the neural plate as the diagram of His indicates that it does, a simple diagram (fig. 6) will serve to make clear what are the conclusions to which in

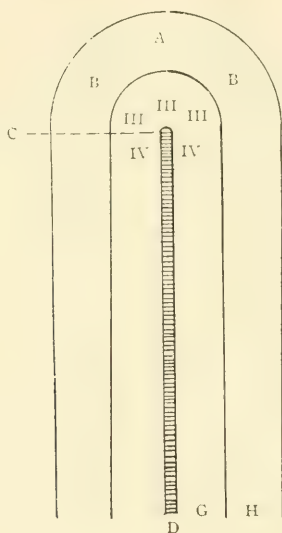


Fig. 6 Diagram to illustrate the interpretation of the cephalic portion of the neural plate. *A.*, the region of the retinal area(s); *B.*, the region of the olfactory lobes (and cerebrum); *C.*, cephalic end of the floor-plate or sutura neurochordalis (fovea isthmi in the neural tube); *D.*, the floor-plate (sutura neurochordalis); *G.*, primary motor zone, lamina basalis; *H.*, primary sensory zone, alar plate; *III*, *N. oculomotorii*; *IV*, *N. trochlearis*.

my opinion one is logically led, both from fact and from theory. In the diagram it will be noted that the alar plate and the basal plate, primary sensory and motor zones, are indicated as extending around from side to side 'anterior' to the cephalic end of the floor-plate or neurochordal suture at whose cephalic end the fovea isthmi appears in the neural tube. The retinal area occupies the more cephalic portion of the alar lamina while the nucleus oculo-

motorius similarly occupies the preaxial portion of the basal plate with the nucleus trochlearis immediately caudad of it. The olfactory areas (and cerebral areas) in the alar plate would occupy positions morphologically caudad of the retinal area. It by no means follows that these areas are more than potentially present in the neural plate. It would be useless, of course to attempt to assign even relative locations for other brain regions without ascertaining the effects that the great growth, in length and breadth, and also the unequal growth, would have.

Certain comments may be made on the relations outlined by the diagram and what they signify.

1. The experiments of W. H. Lewis and Stockard have shown that the retinal area (or areas) occupy the extreme cephalic portion of the neural plate. There is not agreement as to whether the area is primarily single or double, but this has little significance in the present connection, although, if I may state it, my individual opinion is that the evidence supports Stockard's contention of a primarily single medial retinal area in the neural plate. Johnston, from purely morphological studies, has indicated that the cephalic boundary of the neural plate marks the site of the future optic chiasma behind which as the retinal areas separate the primitive optic furrow remains.

2. The closer allocation of the motor and sensory sides of the visual apparatus than would be otherwise possible is also quite suggestive and renders somewhat more comprehensible a feature of head morphology otherwise obscure. 3. The eyes thus would represent the most anterior of the series of sense-organs. This is, I think, no new interpretation, borne out as it is by the reversed relation of eye to olfactory organ in Cyclopia. It also serves to render more comprehensible the seriation of sense organs—retinal, olfactory, otic, etc.—which Duval ('00) so nicely set forth in diagrammatic form in his figure 420.

4. Possibly, though perhaps not probably, the existence of a nucleus centralis n. oculomotorii, effecting a confluence of the oculomotor nuclei of the two sides, may be thus accounted for, as well as the medial position of other nuclei in this region (n. centralis superior, n. centralis raphae, ganglion interpeduncu-

lare). The partial decussation of the oculomotor nerve (crossed origin) might also express a primitive continuity across from side to side in this region.

5. I venture again to call attention to the conclusion of Johnston that what His termed the recessus infundibuli (Basilarleiste) should more appropriately be termed the primitive optic furrow and that the recessus infundibuli was a secondary out-pocketing of the wall of the neural tube. Under the conception of the brain-plate here outlined, this would occur medially between the alar and basal plates separating the sensory zone in the floor (the optic chiasma) from the motor (the floor of the midbrain); but whether at the expense of the sensory zone or of the motor zone or as an essential separation of them, cannot be said. The development of the infundibulum is, I think, unquestionably bound up with the development of the hypophysis, and until the early morphogenesis of the latter is clarified and its morphological significance better estimated, nothing can be added to a mere statement of fact.

6. Such a conception as this of the cephalic portion of the neural plate, it must be conceded, contradicts certain generally accepted doctrines of fundamental brain morphology. Thus, the boundary between primary motor and sensory zones, which appears in the more caudal portion of the neural tube as the sulcus limitans, frequently to be seen, particularly in the mammalian neural tube and in the rhombencephalon, would not terminate at the preoptic recess as is generally thought to be the case, but would terminate in the primitive infundibular recess, primarily continuous across from side to side. In the His models of the developing human brain, as Schulte and Tilney point out, the sulcus limitans does so terminate anterior to the midbrain floor (i.e., in the mammillary region). It is in my opinion a valid objection to the generally accepted interpretation that it includes in the basal, primary motor lamina optic chiasma and hypothalamus—regions which possess no such significance. The motor zone ceases with the floor of the midbrain. This is, I think, more striking in the brain of a lower vertebrate than it is in that of a higher form. The divisions of the brain would lose their

significance as fundamental segments of the neural tube. The telencephalon and diencephalon would then be entirely developed out of alar-plate material. This is the interpretation of Schulte and Tilney ('15).

7. The conception of the floor-plate as marking a line of blastoporic concrescence, and representing the neural portion of a neurochordal suture postulates that when first formed the notochord and floor-plate be coextensive. It would thus be possible to speak of a prechordal portion of the neural plate as a primitive condition, as well as pre- and epichordal parts of the neural tube.

Ahlborn ('83), in the lamprey, so divided the brain into epichordal and prechordal regions, basing the distinction drawn upon three things: 1) The epichordal brain alone possesses nerves comparable to those of the spinal cord; such are lacking in the prechordal portion. 2) It possesses a raphé which is completely lacking in the prechordal brain. 3) It is coextensive with the notochord. Ahlborn thus included only the rhombencephalon in the epichordal brain, the mesencephalon and prosencephalon being prechordal. Strong ('16), doubtless through an appreciation of the force of the first of Ahlborn's points, has likewise divided the brain into epichordal and prechordal parts,⁸ but includes the mesencephalon in the epichordal brain, and the reason for this is obvious; to the midbrain belong the oculomotor and trochlearis nerves. The plan of brain morphology here outlined limits the epichordal brain more nearly to the rhombencephalon, essentially as was done by Ahlborn, in the lamprey. The difficulty in recognizing a motor zone cephalad of the chorda is, however, obviated. I also see no reason why the nuclei of the IIIrd and IVth cranial nerves might not vary in position in

⁸ (P. 453.) "After closure (of the neural tube), in many Vertebrates at least, a three-fold division can be made out: (1) A caudal part of the neural tube, the spinal cord, which gradually expands cranially into (2) the caudal part of the brain (deuterencephalon v. Kupffer) (fig. 400). These two parts lie above the notochord and all the typical cerebrospinal nerves are connected with them. (3) Cranially, at the anterior end of the notochord, the brain wall expands ventrally forming the third portion (archencephalon). At the forward extremity is seen the anterior neuropore. The deuterencephalon is thus an epichordal part of the brain, while the archencephalon is prechordal."

different vertebrates. It is we who draw sharp boundaries, not nature.

It doubtless will be objected that the notochord originally extends farther cephalad than the point which the present interpretation demands, possibly as His thought to the level of the (his) basilar fold. His ('92, 1), in fact, criticised Ahlborn's division of the brain into epichordal and prechordal parts on the ground that the extent of the notochord in the adult is secondary and varies from stage to stage and in different forms. This objection is of course valid; notochord and neural tube grow markedly after they are first laid down and at different rates, but it applies equally to His' own interpretation. Such figures as his own ('92, 2) figure 4, of the torpedo embryo, as well as such carefully constructed figures as those of Scammon ('12) for *Acanthias*, among others, indicate that the notochord in early stages, when first formed, does not extend forward to the basilar fold as the His interpretation demands.

It is evident, however, that our knowledge of the morphological relations at the anterior end of the notochord is quite inadequate, and any consideration would involve the interpretation not only of the notochord and neural plate, but as well the protochordal or prechordal plate, so-called preoral entoderm (cephalic entoderm), etc.; in fact, all aspects of that intensely interesting portion of the head in the immediate neighborhood of the hypophysis. The present interpretation has the merit of recognizing the distinction of epichordal and prechordal portions of the brain tube as primary and not secondary, and of offering an explanation of the significance of this distinction.⁹

⁹ In terminating this paper the writer wishes to acknowledge the helpful editorial comments of Prof. C. J. Herrick.

SUMMARY

1. A differentiated floor-plate extends no farther forward than the fovea isthmi. Increased morphological significance is believed to attach to this depression.

2. The plan of arrangement of the longitudinal zones of His as set forth by him and generally accepted is interpreted as giving a wrong morphological basis for the brain.

3. Theoretic considerations based partly on the 'blastopore theory' indicate: *a*) that the floor-plate corresponds to a suture *neurochordalis* (His); *b*) that the floor-plate and notochordal plate are primarily coextensive; *c*) that the neurochordal suture does not extend to the anterior end of the neural plate; *d*) that the primary motor and sensory zones are continuous from side to side cephalad of the anterior end of the floor-plate.

4. The following interpretations are accepted: *a*) that the optic chiasma marks the anterior end of the neural plate; *b*) that the motor zone terminates with the midbrain; *c*) that the floor-plate terminates at the fovea isthmi; *d*) that the boundary between motor and sensory zones terminates near the mammillary recess.

5. A rational basis for the division of the brain into epichordal and prechordal portions is afforded by the interpretation presented.

6. A number of facts of cephalic and encephalic morphology may be better interpreted on the basis suggested in this paper.

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PLATE 1

EXPLANATION OF FIGURES

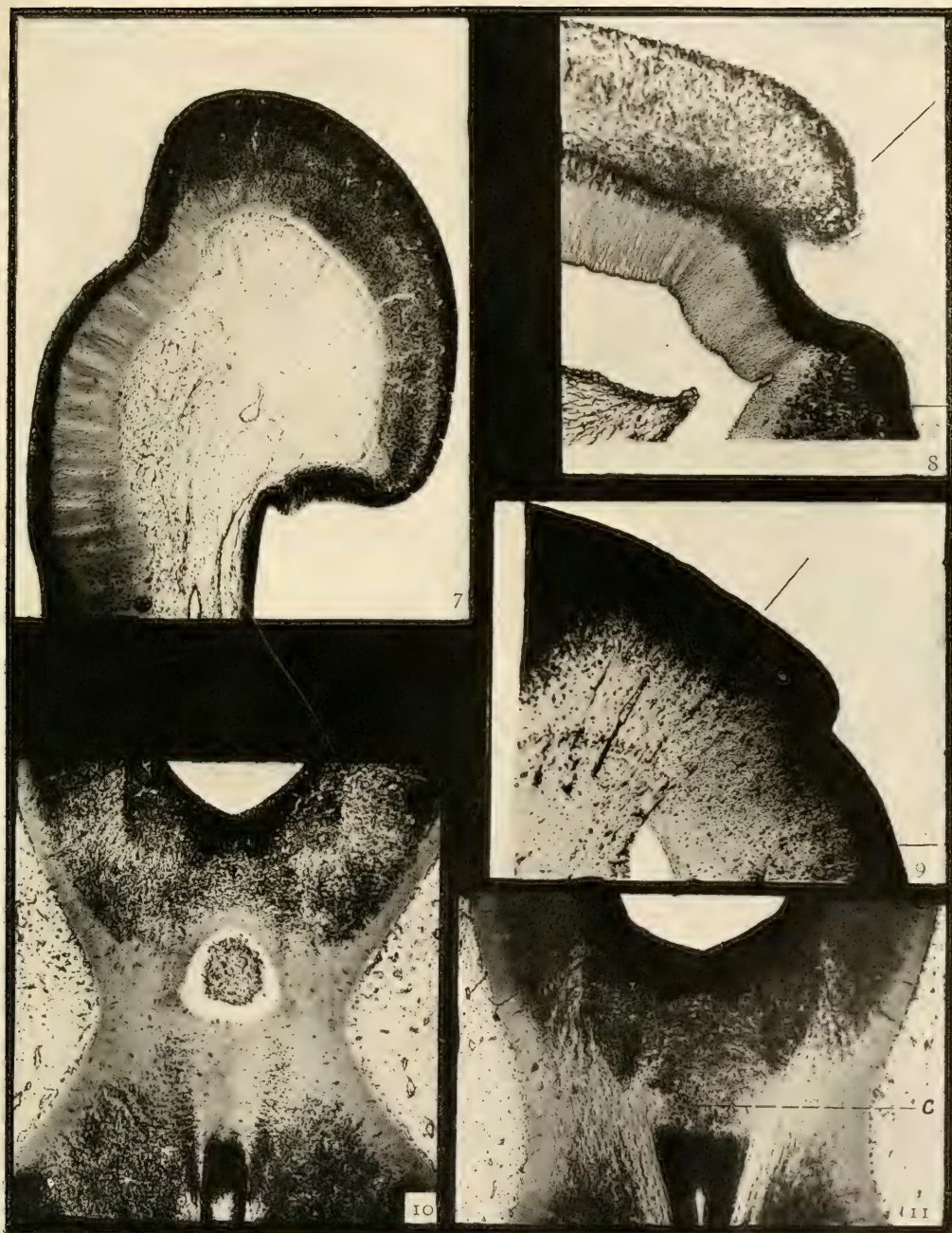
7 Photograph of the median plane in the floor of the brain at the plica encephali ventralis. The section is nearly medial throughout. The floor plate is on the left, extending to the fovea isthmi. Compare with figure 3. Calf, 23 mm. $\times 37\frac{1}{2}$.

8 Photograph of the floor of the brain of the shark, *Squalus acanthias*, 40 mm. length, at the fovea isthmi. Only the region included between the two lines is median. Note the sudden cessation of the floor-plate, its characteristic structure in comparison with the floor of the midbrain. Compare with figure 1 and also with figure 7. $\times 67\frac{1}{2}$.

9 Photograph of the floor of the brain of the chick, seven and one-half days' incubation, at the fovea isthmi. Only the region included between the two lines is median. The cephalic side, as in figure 2, is toward the left. $\times 67\frac{1}{2}$.

10 Photograph of a section cutting horizontally the floor of the brain at the plica encephali ventralis through the summit of the included mesenchyme (i.e., the fossa interpeduncularis). Calf, 20 mm. (Cornell Univ. series C.21). $\times 37\frac{1}{2}$.

11 Photograph as in figure 10, but seventeen sections (170μ) farther dorsal, where 'C' marks the upper end of the floor plate. In figures 10 and 11 the cephalic side is up. $\times 37\frac{1}{2}$.



Resumen por el autor, Edward Phelps Allis.
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Las ramas de los nervios branquiales de los peces, con especial
mención de *Polyodon spathula*.

En *Polyodon* y *Polypterus*, y probablemente en todos los peces, los nervios branquiales en apariencia poseen las ramas siguientes: una rama faríngea, ramas pretremáticas externas e internas, ramas postremáticas externas e internas, y una rama dorsal s. supratemporal. La rama postremática externa está formada por tres cordones paralelos y distintamente independientes, que pueden denominarse anterior, medio y posterior. El posterior contiene todas las fibras motrices del nervio, mientras que los otros están formados por fibras comunes, sensoriales generales, y simpáticas o latero-sensoriales que se encuentran en proporción variable en diversos nervios. Las fositas nerviosas, llamadas poros primitivos en *Polyodon*, están inervadas por nervios que en su mayor parte son latero-sensoriales. Estas fositas están ciertamente relacionadas filogenéticamente con las ampollas de los selacios, pero también parece cierto que no responden a los estímulos de la presión, como ocurre con las de los selacios, según se cree. Las costumbres y hábitat de *Polyodon* y la distribución de las fositas parecen indicar que son órganos o del gusto o táctiles, y más probablemente del gusto, pero en ambos casos el origen central de las fibras que las inervan no corresponde con el de las fibras del sentido correspondiente de los Teleostomos. Si son órganos gustativos, este sentido se ha desarrollado en diferentes peces en relación con dos series de fibras nerviosas claramente diferentes o bien las fositas nerviosas y los botones terminales deben estar relacionados filogenéticamente.

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THE BRANCHES OF THE BRANCHIAL NERVES OF FISHES, WITH SPECIAL REFERENCE TO POLYODON SPATHULA

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A branchial nerve was long considered to have but three typical branches, a ramus posttrematicus, a ramus pretrematicus, and a ramus pharyngeus. The rami posttrematicus and pretrematicus were said to both lie along the convex, and hence external surface of the branchial bar of the arch to which they are distributed, the ramus pretrematicus lying in the arch next anterior to the ramus posttrematicus, and posterior and parallel to the ramus posttrematicus of that arch. Stannius ('49) found, in nearly all of the many fishes examined by him, the basal portions of the rami pretrematicus and pharyngeus of the nervus glossopharyngeus fused with each other for a certain distance, thus forming a so-called ramus anterior s. hyoideus, but he makes no mention of similar fusion in any of the other nerves. The ramus posttrematicus of each branchial arch is said by him to send an important branch or branches to the dermal tissues that cover the anterior surface of the branchial bar of the arch, but neither this branch nor the rami dorsales of the nervi glossopharyngeus and vagus are spoken of as typical branches of a branchial nerve.

In 1911 Sewertzoff recognized and described what he considered to be a fourth typical branch of a branchial nerve, and as it is pretrematic in position and lies along the concave, and hence internal, surface of the arch to which it is distributed, he called it the ramus pretrematicus internus, the ramus pretrematicus of earlier descriptions then becoming the ramus pretrematicus externus. Sewertzoff gives me credit for having shown, in one of my drawings of *Amia* (Allis, '97, fig. 59, pl. 35),

this pretrematicus internus branch of the first three vagus nerves, and he says in a foot-note that it is described, but not specifically named, by Bender ('06) in several of the Selachii and Batoidei, and in Polypterus and Ceratodus. That branch of the ramus posttrematicus of each branchial arch that is said by Stannius to be distributed to the dermal tissues on the anterior surface of the arch to which it is related is not described by Sewertzoff, nor shown in his figure. In *Amia*, I (Allis, '97) found it running downward along the anterior surface of the epibranchial of the arch to which it belongs, and reaching and being distributed to the internal surface of the ventral half of that arch. It will accordingly be hereafter referred to as the ramus posttrematicus internus.

In work that I have under way on *Polypterus*, the glossopharyngeus and first two vagus nerves each has the four so-called typical branches of Sewertzoff's descriptions, and also the ramus posttrematicus internus; and their homologues, in somewhat modified condition, are found on the facialis and third vagus nerves, and apparently also on the trigeminus. A ramus dorsalis is also apparently found on both the facialis and trigeminus, as well as on the glossopharyngeus and vagus, and in addition to these six branches I find, in each branchial arch, a nerve running downward in its arch anterior and parallel to the ramus posttrematicus. This nerve is apparently a branch of the ramus anterior, and not of the ramus posttrematicus, and for reasons to be later given may be called the ramus posttrematicus anticus.

Having found, in *Polypterus*, these several branches on each of the branchial nerves, and also finding them shown, in *Amia* (Allis, '97), on the first vagus nerve, it seemed as if they might all be typical branches. I accordingly had them traced in two series of transverse sections of *Polyodon*, both specimens approximately 140 mm. in length, and also in a single adult, this work all being done by my assistant, Mr. John Henry.

In the two small specimens of *Polyodon*, the roots of the nervi vagus and lineae lateralis issue together through the vagus foramen, and there are no intracranial ganglion cells on either

of them. The vagus root contains general sensory, communis, and motor fibers, and becomes united with the root of the lineae lateralis vagi inside the cranial cavity. From this root an intracranial branch is given off, this branch arising from the dorsal surface of the root, in the line between its communis and general sensory portions, and it is impossible to tell, in my specimens, of what fibers it is composed. The branch, on both sides of the head of one specimen and on one side of the other, runs upward in the cranial cavity, perforates the cartilage, and joins and anastomoses completely with a closed circuit formed by the anastomosis of branches of the rami supratemporalis vagi, supratemporalis glossopharyngei, and oticus trigemini. On the other side of the one specimen the branch is joined by a branch that arises from the general sensory ganglion of the vagus, the branch so formed then joining the ramus supratemporalis vagi. No ganglion cells could be found in the root of the nervus vagus at, near, or anterior to the point of origin of this branch, and no cells are found at any point along the branch, the branch thus apparently having no ganglion cells related to it and apparently agreeing in this with the nerves of *Amphioxus*.

After giving off the above-described intracranial branch, the combined roots of the nervi vagus and lineae lateralis traverse the vagus foramen, which gives passage also to a vein which falls into the vena jugularis, and to a small artery which arises from a dorsal branch of the first efferent branchial artery, the vena jugularis lying ventral to the root of the nerve. As the root traverses its foramen, ganglion cells form on the general sensory fibers, and from it four bundles of fibers arise. One of these bundles runs forward along the lateral surface of the chondrocranium and, separating into two parts, anastomoses with the general sensory and communis components of the nervus hyomandibularis facialis as that nerve issues from its foramen. This branch lies morphologically internal to the hyomandibula and hence is not the homologue of the anastomosis, found in *Amia* and certain of the Teleostei, between the ramus supratemporalis vagi and the ramus opercularis facialis. A second bundle of fibers is sent to the ramus supratemporalis vagi, a

third bundle to the nervus lineae lateralis, and a fourth to the extracranial communis ganglion of the complex. The fibers of the latter bundle lie in the deeper part of the ganglion, in contact with the main sympathetic nerve, and it is impossible to trace the two sets of nerves independently. The combined fibers separate into two bundles which run to or toward two sympathetic ganglia described immediately below.

The communis ganglion is an elongated structure, the anterior portion of which is enlarged to form an independent ganglion for the first vagus nerve, while the posterior portion separates imperfectly into three parts which are related, respectively, to the second, third, and fourth vagus nerves. On the ventral surface of the ganglion there are two small swellings which represent the sympathetic ganglia above referred to, one related to the first vagus ganglion and the other to the second, third, and fourth ganglia. From the communis ganglion fibers are sent to the ramus supratemporalis, the nervus lineae lateralis, and the several vagus nerves, and from the sympathetic ganglia fibers are sent to the several vagus nerves. These latter fibers are quite probably in part general sensory, but as this could not be definitely established, they will be referred to as sympathetic.

The ramus supratemporalis contains general sensory, communis, and lateralis fibers, and certain of its branches form, on the dorsal surface of the chondrocranium, a closed circuit with branches of the ramus oticus facialis and the ramus supratemporalis glossopharyngei. No branch of the nerve forms an anastomosis with branches of the ramus opercularis, as occurs in *Amia* and the Teleostei.

The first vagus nerve is represented by several branches which arise independently from the first vagus ganglion. One of these branches is a communicating branch from the first vagus ganglion to the glossopharyngeus ganglion, and it contains both communis and sympathetic fibers, the latter doubtless being accompanied, as above explained, by general sensory ones. A second branch, also accompanied by sympathetic fibers, separates into two parts, one of which is the ramus pharyngeus and the other the ramus pretrematicus internus. The ramus phar-

yngeus runs forward ventral to the pharyngobranchial of the first branchial arch, and can be traced to the transverse plane of the foramen for the ramus palatinus facialis. The ramus pre-trematicus internus reaches the internal (concave) surface of the first branchial arch and continues onward in that position, lying along the posterior surface of the internal edge of the branchial bar. A third branch, also accompanied by sympathetic fibers, is the ramus pretrematicus externus, which runs forward and reaches the external (convex) surface of the first branchial arch, distal to the surface of insertion of the levator muscle of that arch. There it passes internal to the ramus posttrematicus posticus of the nervus glossopharyngeus and joins the ramus posttrematicus medius, where it continues onward lying close against the posterior surface of the latter nerve. The remaining three branches of the first vagus together form the ramus posttrematicus, and they may be called, because of their relations to each other, the rami anticus, medius and posticus, the ramus anticus receiving a bundle of sympathetic fibers. The rami anticus and medius are both wholly sensory nerves, and run outward external, and hence anterior, to the levator muscle of their arch, the ramus posticus, which contains all the motor fibers of the nerve and but few, if any, sensory fibers, running outward posterior to the latter muscle. All three of these nerves run downward along the external (convex) surface of the branchial bar of the second branchial arch, the ramus anticus lying anterior to the efferent artery of that arch, and the rami medius and posticus posterior to that artery. The ramus medius, while still in the upper (proximal) half of its arch, gives off a ramus posttrematicus internus, this nerve being a wholly sensory one which runs downward along the anterior surface of the epibranchial of the arch, sends a recurrent branch upward along the internal edge of that bar, and then itself reaches the internal edge of the ceratobranchial of the arch. There it sends a large branch downward anterior to the adductor muscle of the arch, along the anterior surface of the ceratobranchial, and itself passes posterior to the adductor muscle, along the internal edge of the ceratobranchial, where it is joined by, and closely

accompanies, or anastomoses with, the ramus pretrematicus internus of the second vagus, the nerve so formed continuing onward through the arch. The ramus posticus first sends a motor branch to the levator muscle of the arch and then one to the adductor muscle, the latter branch running downward on the posterior surface of the epibranchial, as Danforth ('13) has stated. The nerve then continues onward in its arch and innervates the muscles at its ventral end.

The second and third vagus nerves arise from their respective ganglia and have branches that correspond strictly to those above described for the first vagus, the communicating branches from the third ganglion to the second, and from the second to the first, apparently being represented by parts of the large communis ganglion. The fourth vagus nerve also has all these several branches in addition to the large ramus intestinalis.

The root of the nervus glossopharyngeus apparently contains only motor and communis fibers, but it receives an intracranial branch from the root of the nervus lineae lateralis. The root issues from the cranial cavity through an independent foramen and passes ventral to the vena jugularis, a ganglion then immediately forming upon it. On the ventral surface of this ganglion, and partly imbedded in it, there is a small sympathetic ganglion which receives the communicating branch from the first vagus ganglion, above described. From this communis ganglion a supratemporal branch arises, and contains, in addition to communis fibers, all the lateralis fibers of the nervus. It runs dorsally, mesial to the vena jugularis and then along the lateral surface of the chondrocranium, anastomoses with the closed circuit formed by the ramus oticus facialis and the ramus supratemporalis vagi, and is distributed to certain of the laterosensory organs of the main infraorbital laterosensory canal and to adjacent nerve pits.

From the anterior end of the glossopharyngeus ganglion a ramus pharyngeus arises, and soon separates into two parts. One of these parts anastomoses with a branch of the ramus palatinus facialis which issues from the chondrocranium by an independent foramen, the fibers of the glossopharyngeus appar-

ently running proximally along the branch of the palatinus facialis to enter the ganglion formed on the root of the latter nerve. The other part of the ramus pharyngeus runs forward and anastomoses in large part with branches of the main ramus palatinus facialis which are given off after that nerve issues from its foramen. The first-mentioned one of these two parts of the ramus pharyngeus glossopharyngei would thus seem to be in part a communicating branch between the ganglia of the glossopharyngeus and facialis nerves, and is apparently the so-called Jacobson's anastomosis of the Teleostei. From it a branch is given off which unites with a branch that arises from the base of the ramus pharyngeus, the nerve so formed running downward along the anterior edge of the internal surface of the hyomandibula, and, near the distal end of that element, turning downward across the internal (morphologically posterior) surface of the symplectic of Bridge's ('79) descriptions and then forward along the dorsal, and hence morphologically internal, edge of the ceratohyal, this nerve thus being the ramus pretrematicus internus glossopharyngei. From the base of the ramus pharyngeus a nerve is given off which runs outward to the internal surface of the musculus retractor hyomandibularis of Danforth's ('13) descriptions, and there turns downward and backward along that surface of that muscle, lying approximately internal to the dorsoposterior edge of the hyomandibula. At the distal end of the hyomandibula it closely approaches the ramus hyoideus facialis and then turns downward along the internal (morphologically posterior) surface of the interhyal and then forward along the internal (posterior) surface of the ceratohyal. This branch of the glossopharyngeus is thus a ramus pretrematicus externus, and its relations to the hyomandibula are in accord with my conclusion (Allis, '18) that that cartilage is a branchial-ray bar, and not an element of the branchial bar of the hyal arch. Seven other nerves arise from the glossopharyngeus ganglion, in the one adult specimen examined, all but two of them uniting to form a ramus posttrematicus anticus, the other two being the rami medius and posticus posttrematicus. The ramus posticus contains all the motor

fibers of the nerve and runs outward posterior to the levator muscle of the arch, the rami medius and anticus running outward anterior to that muscle. The ramus medius is closely accompanied by the ramus pretrematicus externus of the first vagus, and gives off a ramus posttrematicus internus; all of these nerves having courses similar to those of the corresponding nerves in the more posterior arches.

The facialis-acusticus complex has a motor, a communis and two lateralis roots, and a fifth root, which is small, arises between the motor and the posterior one of the two lateralis roots and is quite certainly general sensory, though this could not be definitely established. The communis root immediately separates into two parts, and on these two parts, and on the two lateralis roots, a large intracranial ganglion forms, the communis part of the ganglion lying ventral to the lateralis one. From the anterior portion of the ganglion the rami oticus, buccalis, and ophthalmicus superficialis arise, all of them containing both lateralis and communis fibers, and if these nerves belong to the nervus trigeminus, as I believe, the anterior lateralis root, and the anterior portion of the communis root, must also belong to that nerve. Communis fibers, but no lateralis ones, are also sent from the anterior portion of the ganglion to the rami mandibularis and maxillaris trigemini. From about the middle of the length of the ganglion the ramus palatinus facialis arises, composed entirely of communis fibers, and from its posterior portion both lateralis and communis fibers are sent to the nervus hyomandibularis facialis. From the posterior one of the two lateralis roots, close to its base, the nervus acusticus arises, and receives a bundle of fibers from the small and apparently general sensory root, the acusticus thus apparently corresponding, in its relations to the nervus facialis, to the rami supratemporales of the glossopharyngeus and vagus nerves. The remainder of the small and apparently general sensory root then, in three out of four cases examined, runs through the ventral portion of the lateralis-communis ganglion into the ramus hyomandibularis facialis, while in the fourth instance a part, only, of the nerve has that course, the remainder turning forward in the ganglion and there being lost.

The ramus hyomandibularis facialis issues from the cranial cavity by a separate foramen and enters the facial canal of Bridge's ('79) descriptions, that canal being also traversed by the vena jugularis, the arteria carotis externa, and a lymph vessel. The nerve contains motor, lateralis, and communis fibers, and also a bundle of the apparently general sensory fibers above referred to, and as these several kinds of fibers occupy definite regions of the nerve, the approximate composition of the larger branches of the nerve could be determined. On issuing from the facial canal the nerve immediately receives, or sends fibers into, the communicating branch, already described, from the general sensory component of the vagus ganglion, this communicating branch apparently receiving all the general sensory fibers of the hyomandibularis together with some of its communis fibers. The nerve then runs posteriorly internal to the hyomandibula and there gives off its ramus opercularis, which contains both lateralis and motor fibers. This branch runs posteriorly on the external surface of the musculus retractor hyomandibularis of Danforth's ('13) descriptions, the motor fibers going to that muscle and the lateralis ones to the little organs called by Collinge ('94) primitive pores, but which, for reasons given below, I shall refer to as nerve pits. The ramus hyomandibularis then passes across the dorsoposterior edge of the hyomandibula and separates into its two branches, the rami hyoideus and mandibularis. The ramus hyoideus contains both lateralis and motor fibers and runs downward along the posterior (morphologically external) edges of the cartilages of the hyal arch, the lateralis fibers going to nerve pits on the gill cover. The ramus mandibularis turns downward along the lateral (morphologically anterior) surface of the hyomandibula, and there separates into its internal and external branches. The ramus externus contains all the remaining lateralis fibers of the nerve, and runs downward along the lateral surfaces of the symplectic and interhyal of Bridge's ('79) descriptions, and then forward ventromesial to Meckel's cartilage, sending branches to the organs of the hyomandibulo-mandibular laterosensory canal and to certain of the nerve pits on the ventral surface of the

lower jaw. The ramus internus is composed entirely of communis fibers, and contains most, if not all, of those fibers of the nerve.

The ramus hyoideus facialis is thus either simply the ramus posttrematicus posticus of the nervus facialis, or that ramus plus the ramus medius; the ramus mandibularis externus is either the ramus posttrematicus anticus alone, or that nerve plus the ramus medius, and the ramus mandibularis internus is the ramus posttrematicus internus.

The ramus palatinus facialis separates while in the cranial cavity into two parts, which issue from the cranial cavity by separate foramina. The posterior branch is the smaller of the two, and, as already stated, anastomoses completely with a branch of the ramus pharyngeus glossopharyngei to form a communicating branch between the ganglia of the nervi glosso-pharyngeus and facialis which apparently corresponds to the Jacobson's anastomosis of the Teleostei. The anterior and larger portion of the palatinus issues through an independent foramen and forms the ramus palatinus properly so called. Running forward, it sends a small branch outward over the dorsomesial edge of the palatoquadrate to join and fuse with the ramus mandibularis trigemini, and two or three branches downward internal to the palatoquadrate; the former branch being the ramus pretrematicus externus facialis and the others, together, forming the ramus pretrematicus internus, usually called, in current descriptions of other fishes, the ramus palatinus posterior. The remainder of the ramus palatinus is then the ramus pharyngeus facialis and runs forward in the roof of the buccal cavity.

The nervus facialis thus has all the branches typical of the more posterior nerves, but it differs from them and also from the nervus trigeminus in that its ramus posttrematicus contains lateralis fibers. These fibers must therefore be either pre-existing fibers that have undergone both change of function and change of central origin, or fibers that have invaded this arch, as the nervus lineae lateralis invades the body of the fish, by following a patch of sensory tissue which has given rise both to

the nerve hillocks of the laterosensory canals and to the sensory cells of the nerve pits. Nachtrieb ('10) maintains that there are no sensory cells related to these pits, and says that he never found any of the branches or branchlets of the lateral-line nerves in any way in communication with them. He accordingly considers the pits to be simply secretory organs secreting a peculiar mucus. Kistler ('06) had, on the contrary, previously found what he considered to be nerve fibers going directly to the cells at the bottoms of the pits, and my work confirms this statement, for I find, both in the adult and in the 140-mm. specimens, nerve fibers going directly to the bottom of each of the many pits that were examined. Furthermore, no trace of mucus was found in any of the pits of the 140-mm. specimens. It therefore seems certain that these pits are, in part at least, sensory organs, and it is equally certain that the nerves that innervate them are quite largely composed of lateralis fibers. The branches that supply the organs on the gill cover arise, however, from the rami opercularis and hyoideus facialis, and not from the mandibularis externus, which supplies all the sensory organs in the hyomandibulo-mandibular laterosensory canal. The branches here concerned of the ramus opercularis apparently correspond to that branch of the ramus opercularis superficialis facialis of Herriek's ('99) descriptions of *Menidia* that supplies what that author describes as small and scattered pit organs, but I know of no fish in which the ramus hyoideus contains lateralis fibers, unless it be *Ameiurus*. Herriek ('01) says of the latter fish that the ramus hyoideus apparently only contains motor and general sensory fibers, but adds that there are occasional terminal buds and small pit organs in the branchiostegal membrane which may be supplied by branches of this nerve, though he could not trace fibers to them. In *Gadus*, Herriek ('00) describes a nerve which he says is clearly formed by the fusion of the rami opercularis superficialis and hyoideus, and a minute twig of this nerve is said to run downward, overlying the ramus hyoideus, and to be distributed to pit organs.

From the above it is seen that the nerve pits on the opercular gill of *Polyodon* and the small pit organs of *Ameiurus* have mark-

edly similar innervations, and transverse sections of the two organs, as shown by Herrick ('03) and Kistler ('06), are somewhat similar. The nerve pits of *Polyodon* are found in little groups, and certain of the pits in each group are arranged in little clusters, the group apparently having been formed, as suggested in my work on the lateral canals of this fish (Allis, '03), by the complete subdivision of a single primitive pit into several independent pits, and the subsequent incomplete subdivision of these secondary pits to form the little clusters above referred to. If one of these little clusters were to sink beneath the surface, it would apparently give rise to a nerve sac such as is found in *Acipenser*, for Merkel ('80) says that a large proportion of these nerve sacs open on the external surface by a number of pores lying close together. These nerve sacs must closely resemble the ampullae of *Chlamydoselachus*, for these ampullae are, as Merritt Hawkes ('06) has stated, pear-shaped structures which lie immediately beneath the dermis and are formed by little packets of from two to six simple ampullae, all of these simple ampullae having short tubules which open independently, but close together, at the bottom of a slight depression on the outer surface of the skin.

It would therefore seem quite certain that the nerve pits of *Polyodon* are a primitive form both of the nerve sacs of *Acipenser* and the ampullae of the *Selachii*, and it is for this reason that I have called them nerve pits, instead of either pit organs or primitive pores. It would also seem as if these nerve pits, and hence also the *Selachian* ampullae, must be represented, in the *Teleostei*, by the small pit organs of Herrick's descriptions, and the latter author has already suggested this homology for the ampullae ('03, p. 135). This being so, it would be natural to assume that the nerve pits and small pit organs should respond to the same stimulus as the ampullae, which, according to Metcalf ('15), is that of pressure, the function of the ampullae being to inform the fish of the depth of the water in which it is swimming, the direction of currents, and possibly also of the presence of vibrations of low frequency ('deeper notes'). The habits and habitat of *Polyodon* are, however, opposed to this assumption.

Polyodon is said by Jordan ('05) to be a bottom feeder of sluggish habits, and its long snout is said to be more or less sensitive and to be used to stir up the mud in which are found the minute organisms on which the fish feeds. The fish abounds in the Mississippi, which is always a markedly muddy river, and *Psephurus*, a closely allied species, is found in the Yangtse and Hoang Ho, which are also muddy rivers. Vision can therefore be of but relatively little value to these fishes, and, in accord with this, the eyes of *Polyodon* are small. This lack of visual power should then be compensated for by some other sense, if the fish is not to be too severely handicapped in its search for food, and the nerve pits seem to have been developed for this purpose. What their function is, can, of course, only be determined by experiment, but response to pressure would here seem to be of little, if any, value, while a keen sense of either touch or taste would be of great advantage; but if they respond to either of the latter stimuli, the central origin of the fibers that innervate them would not correspond to that of the fibers that innervate the organs of corresponding sense in the Teleostei. In the numerous catfishes that inhabit the Mississippi and have habits and visual powers similar to those of *Polyodon*, a keen sense of taste has been developed in numerous terminal buds on the external surface of the head (Herrick, '03), but none of these buds could be found anywhere on the external surface of the head of my 140-mm. specimens of *Polyodon* excepting only along the upper and lower margins of the mouth, and but few of them even there. As a few nerve pits (small pit organs) are found on the outer surface of the head of the catfishes, it may be that the conditions there represent the last stages of the displacement of one sense organ by another responding to the same stimulus but better adapted to the purpose.

The *nervus trigeminus* arises by two roots, one motor and the other general sensory, the latter root being connected with the root of the *nervus profundus* by an intracranial bundle of fibers. The motor and general sensory roots run outward ventral to, and wholly independent of, the anterior portion of the intracranial *lateralis-communis* ganglion and issue from the

cranial cavity through an independent foramen, a ganglion beginning to form on the general sensory fibers as they traverse the foramen, but lying in large part beyond it. In addition to the fibers from these two roots, which are currently considered to form the entire nerve, I consider the *lateralis* and *communis* fibers that form the *rami ophthalmicus superficialis*, *oticus*, and *buccalis* to belong to it, these latter fibers all arising from the anterior portion of the intracranial *lateralis-communis* ganglion.

The *ramus ophthalmicus superficialis* contains both *lateralis* and *communis* fibers, issues from the cranial cavity through an independent foramen, and has the usual course through the dorsal portion of the orbit. Close to it, on each side of the two specimens examined in serial sections, a small nerve arises from the *lateralis-communis* ganglion, traverses an independent foramen, and, running forward, either goes directly to nerve pits, or first forms anastomoses with branches of the *ramus profundus* and then supplies those pits or laterosensory organs. This little nerve was not found in the adult.

The *ramus oticus* arises from the intracranial *lateralis-communis* ganglion, and contains both *lateralis* and *communis* fibers. It perforates the lateral wall of the chondrocranium by an independent foramen, runs upward along its external surface, then again traverses a part of that wall, and issues in the bottom of the deep anterior end of the f-shaped groove described by Bridge ('79) on the dorsal surface of the chondrocranium. There it sends a branch to two organs, apparently laterosensory, which lie in a diverticulum of the spiracular canal which traverses the foramen called by Bridge the foramen x. The nerve then separates into two parts, one of which perforates an overhanging ledge of cartilage and innervates certain organs in the main infraorbital canal. The other part enters a canal in the cartilage, sends branches upward, while traversing it, to innervate nerve pits on the dorsal surface of the head, and issues from it at the dorsal edge of the articular facet for the hyomandibula to there anastomose completely with the supratemporal branches of the glossopharyngeus and vagus nerves. This *ramus oticus* is quite certainly a branch of the *buccalis*, and must be either a

recurrent branch similar to those recurrent branches of the *nervus mandibularis externus facialis* that are sent to the organs in the dorsal portion of the hyomandibular laterosensory canal, or be the serial homologue of the *rami supratemporales* of the *glossopharyngeus* and *vagus* nerves.

Close to the *ramus oticus* another branch arises from the *lateralis-communis* ganglion, contains both *lateralis* and *communis* fibers, and issues from the cranial cavity by a separate foramen in the lateral wall of the chondrocranium. It then runs upward for a short distance along the lateral wall of the chondrocranium, again traverses the cartilage of the chondrocranium, and issues on its dorsal surface in the bottom of the deep anterior end of the f-shaped groove above referred to, slightly anterior to the *ramus oticus*. Like that nerve, it then perforates an overhanging ledge of cartilage and supplies certain organs in the dorsal end of the postorbital portion of the main infraorbital laterosensory canal.

The *ramus buccalis*, after having given off the two branches above described, enters the trigeminus foramen along with the general sensory and motor fibers of the *nervus trigeminus*, and while traversing that foramen gives off a branch which, as it issues from the cranium, is separated from the remainder of the nerve by a small bar of cartilage. This branch contains both *lateralis* and *communis* fibers, and separates into branches which are distributed to nerve pits on the upper jaw.

After giving off the above-mentioned nerve, the *ramus buccalis*, containing both *lateralis* and *communis* fibers, issues from the trigeminus foramen and joins the *nervus maxillaris trigemini*, its further course not being traced.

From the extracranial general sensory ganglion of the *nervus* a branch composed of motor and general sensory fibers is sent to the *musculus levator arcus palatini*, and then the nerve separates into its two parts, the *rami mandibularis* and *maxillaris trigemini*. The former contains all the remaining motor fibers of the nerve, together with general sensory fibers, and is certainly a typical *ramus posttrematicus*, notwithstanding that it contains general sensory fibers in place of the *communis* or

lateralis fibers found in the more posterior nerves. The ramus maxillaris, which contains only general sensory fibers, would therefore seem to be a ramus anterior, but as it runs antero-ventrally across the anterior surface of the palatoquadrate, and sends branches to the ventral, and hence morphologically internal, edge of that cartilage, it may contain a part of the ramus posttrematicus internus, the remainder of that nerve being represented by a branch of the ramus mandibularis sent to the dorsal, and hence morphologically internal, edge of Meckel's cartilage. The further course of this nerve was not traced, but if it has branches that correspond to those branches of *Amia* (Allis, '97) that are sent to the external and internal surfaces of the maxilla, they would seem to be the rami pretrematicus externus and internus, the remainder of the nerve being a ramus pharyngeus.

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Las células nerviosas intermusculares de la lombríz terrestre.

1. En la lombríz terrestre existen células nerviosas diseminadas, que probablemente representan vestigios de la red nerviosa primitiva de los invertebrados inferiores. 2. Existen por lo menos cuatro tipos celulares, que difieren por su morfología, en ciertas regiones intermusculares, a saber: En los anillos nerviosos circulares colocados entre las capas musculares longitudinal y circular, y en los nervios periféricos situados dentro de la capa de músculos circulares. 3. De los cuatro tipos celulares, tres de ellos, las células bipolares fusiformes, las semilunares bipolares y las triangulares tripolares, son considerados por el autor como asociados con la porción efectora del sistema nervioso, representando células externas que, en el desarrollo filogenético del sistema nervioso central, no se han incorporado al cordón ventral. 4. El cuarto tipo, formado por células largas, delgadas, piramidales o fusiformes, está contenido casi exclusivamente dentro de la capa muscular circular, pero también envía finos procesos a la epidermis. En su estructura, propiedades colorantes y en su relación con el cordón ventral se asemejan a las células de los órganos sensoriales epidérmicos, habiéndose interpretado como células sensoriales colocadas profundamente.

Translation by José F. Nonidez
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THE INTERMUSCULAR NERVE CELLS OF THE EARTHWORM

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SEVEN FIGURES

INTRODUCTION

The so-called intermuscular nerve-cells of the earthworm have been referred to, usually incidentally, in several papers on the central and peripheral nervous systems of this animal, but in no paper has a complete description of the size, form, distribution, and relations of these cells been attempted. In view of the more or less general acceptance of the annelid theory of the origin of the vertebrates and since several annelids, viz., *Sigalion*, *Nereis* and *Allolobophora*, have been pointed out as exemplifying progressive stages in the transformation of the diffuse peripheral nervous system of the lower invertebrates into the centralized deep-lying system of the higher invertebrates and vertebrates (Parker, '19, pp. 204-5), the writer has thought it worth while to place on record the following observations, based upon a study of a large amount of earthworm material which had been prepared according to well-accredited neurological methods.

In order to eliminate needless description and comment, both in the review of literature and in the presentation of the results of this investigation, it seems advisable at this time to outline briefly some of the main features of the structure of the earthworm nervous system and to explain the descriptive terms which will be used here. From each body somite three pairs of lateral nerve trunks arise, one pair from the sides of the ventral nerve-cord just behind the anterior septum and two pairs, more posterior and close together, from the ganglionic mass itself. These lateral nerve trunks pass ventrolaterally across the body cavity

to the layer of longitudinal muscle fibers, and in this position each gives rise to dorsal and ventral rami. The dorsal rami run between the two muscle layers of the body wall as far as the middorsal line, forming the dorsolateral portions of the so-called nerve ring. From each dorsal portion there is given off first of all branches to the intersetal tract and along the rest of its course dorsally many small peripheral branches pass vertically or obliquely toward the epidermis.

The ventral rami run ventrally in the same relative position as the dorsal ones, extend to the midventral line, and give rise along their course to numerous peripheral branches. In this way three main nerve rings, an anterior, middle, and posterior, are established for each body segment.

In referring to the nerve cells, their locations will be designated in the terms of the preceding description and the direction of their processes will be indicated by the phrases proximal, distal dorsally, distal ventrally, and peripheral, according as the processes extend toward the ventral chain, toward the middorsal line in the dorsal portion of a nerve ring, toward the midventral line in the ventral portion of a nerve ring, and toward the epidermis in a peripheral nerve.

REVIEW OF LITERATURE

Hesse ('94) described groups of ganglion cells in the course of the nerves of the prostomium of the earthworm, but in the nerve rings of the body segments he observed only one nerve cell. It was bipolar. The brief statement by Hesse regarding ganglion cells caused Langdon ('95) to reexamine the material she had studied. As a result of the reexamination she discovered that a series of alum-carminic preparations showed a number of ganglion-cells in the nerve rings and gave in a foot-note the following record for the first thirteen metameres: first metamere, none; second metamere, one on its median nerve ring; third metamere, one on its anterior ring and four on its posterior ring. In metameres three to thirteen, two to eight ganglion cells were found on every nerve ring. All the cells noted were of the bipolar type.

Dechant ('06), by means of intravital methylene blue, succeeded in demonstrating ganglion cells in the nerve rings of the earthworm, but, unfortunately, owing to the fact that he was working with animals which were densely pigmented dorsally, his studies were confined to cells found in the more ventral portions of the earthworm body. For the anterior and posterior nerve rings he found the ganglion cells regularly arranged, usually in groups of three, in the region of the dorsal pair of setae. In the median nerve ring, however, only a single cell was occasionally observed in the vicinity of a setal follicle. The cells were of two types, either spindle-shaped and bipolar or triangular and tripolar. In the tripolar cells two processes lay in the nerve ring, while a third much shorter process passed vertically through the circular muscles toward the epidermis.

More recently tripolar cells have been described by Kowalski ('09) who used Boule's ('07, '09) modification of the silver-nitrate method of Ramón y Cajal for neurofibrillae. Kowalski describes specifically and figures (figs. 60, 61) two tripolar cells which he refers to as 'cellules sensibles profondes tripolaires.' Figure 60 represents a cell in the nerve ring, with two processes lying within the ring itself, while from the outer pole a bundle (*faisceau*) of neurofibrils passes vertically to the epidermis. In figure 61 the tripolar cell lies at the bifurcation of a lateral nerve trunk. One of its processes extends proximally in the lateral trunk while the two others pass distally, one in the dorsal and the other in the ventral portion of the nerve ring.

Boule ('13), in the course of a detailed discussion regarding the evidence in the earthworm of a correlation between the structure of the nerve cells and the direction of conduction of the impulse, refers incidentally to both bipolar and tripolar cells in the lateral nerve trunks and nerve rings. The tripolar cell (fig. 21) corresponds, in its position and in the extension of its processes, with the one figured by Kowalski ('09, fig. 61).

In the following year von Szuts ('14), in an extended account of the finer structure of the central nervous system of the earthworm, failed to make any mention of the tripolar cells observed by Dechant ('06), Kowalski ('09), and Boule ('13). He de-

scribes, however, two types of bipolar cells which are distinguished from one another by the differences in their size and in the arrangement of their neurofibrils. The smaller cells were referred to merely as 'die Nervenzellen' and contained neurofibrils which, although often highly branched, transversed the cell bodies without anastomosing. The large bipolar cells, on the other hand, showed the intracellular fibrils anastomosing to form complex networks and were given the descriptive title, 'die intermuskulären sensorischen Ganglienzellen.' The small cells were observed on the inner side of the nerve ring close to the longitudinal muscles and in the margin of the ventral nerve cord at the point of exit of a lateral trunk. Boule ('13) also shows small bipolar cells in the latter position (fig. 13). Of the large bipolar cells, some were situated in the nerve ring, while others lay entirely within the circular muscle layer.

MATERIAL AND METHODS

Helodrilus caliginosus and *Allolobophora* (*Eisenia*) *foetida*, readily obtained in any market garden, were utilized in this work. All the material studied was taken from the midbody region, somewhat posterior to the clitellum. Very satisfactory preparations were obtained with intravital methylene-blue staining and Boule's modification of the Ramón y Cajal technique for neurofibrils. Intravital methylene-blue staining was secured by means of two methods. Some animals were injected intracoelomically with a 1 per cent solution of methylene blue in normal saline. Others were partially immersed in the solution and allowed to remain in the fluid till they became colored a deep blue. In both cases the color was fixed with Bethe's invertebrate fluid and the tissue imbedded in paraffin and cut in serial sections $20\ \mu$ thick.

For silver impregnation, portions of worms, 5 to 10 mm. long, were fixed in one of Boule's mixtures, usually formula B (formalin, 25 cc.; glacial acetic acid; 5 cc.; ammonia, 0.5 cc.; distilled water, 100 cc.), for from twenty-four to forty-eight hours, impregnated six days in a $1\frac{1}{2}$ per cent silver-nitrate solution at 38°C .

and reduced in a 1 per cent solution of hydroquinone for twenty-four hours. Following routine procedure, the tissue was sectioned and mounted in balsam, with cover-glasses. Preparations left uncovered were found to deteriorate very rapidly. The pyridine-silver method of Ranson, and Ramón y Cajal's technique unmodified were also tried, but did not yield so uniform and excellent results as the method just outlined.

Both the methylene-blue stain and Ramón y Cajal's modified silver-nitrate impregnation left the intermuscular cells clearly outlined, although the pictures presented differed greatly. The silver method showed only neurofibrils and left the cell body and nucleus practically colorless, while successful methylene-blue stains colored the entire cell. Since the silver-nitrate method was known to be uniform in its action, it was chiefly relied upon in the determination of the number of nerve cells present in the different regions. Methylene blue, while capricious and discouraging to work with, proved very useful in the tracing of cell processes and in the determination of their relations to other cells and tissues.

THE INTERMUSCULAR NERVE CELLS

All preparations showed both bipolar and tripolar cells, but the number of bipolar cells was greatly in excess of the number of tripolar, the proportion being approximately 5 to 1. The cells did not exhibit any very definite or regular arrangement, but were usually scattered irregularly along the nerve rings. There was, however, in many cases a marked tendency toward grouping in the intersetal tracts.

The number of cells found in the three nerve rings varied considerably. The largest numbers were invariably found in the posterior rings, and the highest record for this location was fifteen, eleven bipolar and four tripolar cells. Next in order came the anterior nerve ring with an average of six cells, while the middle ring usually contained very few cells, five being the maximum observed.

a. Tripolar cells

The tripolar cells are found in locations where branchings of the larger nerve trunks occur; that is, at the bifurcation of the lateral nerve trunks to give rise to the dorsal and ventral rami of the nerve rings and along the nerve rings at the points of origin of the many peripheral nerves; but they are not found uniformly in these positions. This is especially true along the nerve ring, since four or five tripolar cells is usually the maximum number found on any one ring.

The cells approximate a triangular outline. Their nuclei are spherical and in all methylene-blue preparations a well-defined nucleolus and a delicate chromatin network can be distinguished. Silver preparations leave the nuclei unstained, but show a dense network of neurofibrils occupying the bodies of the cells (fig. 1). In most of the tripolar cells the nuclei occupy central positions. When eccentrically placed, however, they are invariably found nearest that pole from which a proximal process arises.

The tripolar cells which are found at the bifurcation of the lateral nerve trunk do not always bear the same relations to the nerve system. In some cells, one process extends proximally in the nerve trunk, while the other two processes extend distally and ventrally, and distally and dorsally, respectively, in the nerve ring. In other cells, one process extends proximally, one distally and ventrally and one peripherally. Again in others practically the same relations are maintained as in the second case except that one process, instead of passing ventrally, passes dorsally in the nerve ring. From the tripolar cells, situated at the points of origin of the peripheral nerves, whether in the dorsal or ventral portion of the nerve ring, one process always passes peripherally toward the epidermis while one of the two others passes proximally toward the ventral nerve cord and the other distally toward either the middorsal or midventral line, as the case may be.

The processes passing peripherally were traced readily in many cases to the bases of the epidermal cells, but were lost in the basiepithelial network (Dechant, '06), so that positive evi-

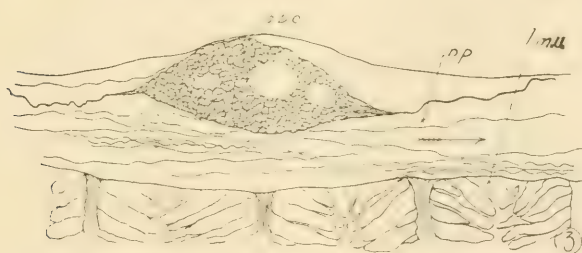
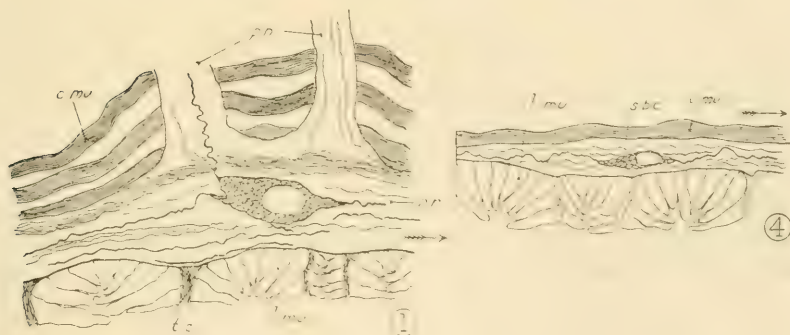
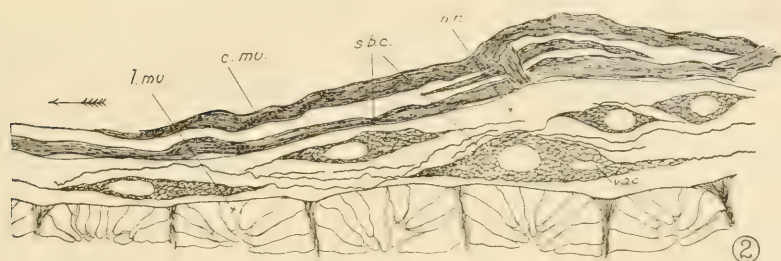


Fig. 1 Tripolar cell in the dorsal portion of a nerve ring at the point of origin of a peripheral nerve. *c.mu.*, circular muscles; *l.mu.*, longitudinal muscles; *n.r.*, nerve ring; *p.n.*, peripheral nerve; *t.c.*, tripolar cell. Ramón y Cajal method modified. $\times 540$. In all figures the arrow points proximally.

Fig. 2 A group of spindle-shaped bipolar cells in the intersetal region of a nerve ring. *c.mu.*, circular muscles; *l.mu.*, longitudinal muscles; *n.r.*, nerve ring; *s.b.c.*, spindle-shaped bipolar cells; *vac.*, vacuole. Ramón y Cajal method modified. $\times 540$.

Fig. 3 Large spindle-shaped bipolar cell in the ventral portion of a nerve ring. *l.mu.*, longitudinal muscles; *n.r.*, nerve ring; *s.b.c.*, spindle-shaped bipolar cell. Ramón y Cajal method modified. $\times 540$.

Fig. 4 Small spindle-shaped bipolar cell in the ventral portion of a nerve ring. *c.mu.*, circular muscles; *l.mu.*, longitudinal muscles; *s.b.c.*, spindle-shaped bipolar cell. Ramón y Cajal method modified. $\times 540$.

dence concerning their possible continuity with intra-epidermal fibers is lacking. In no case, however, was there any evidence of a peripheral bundle of fibers (Kowalski, '09) being given off by a tripolar cell. In many instances numerous fibers were observed running parallel with a peripheral process of a tripolar cell, but they were not connected with the cell itself, and, furthermore, a process of a tripolar cell could usually be easily distinguished from the majority of the fibers in a peripheral nerve by its coarseness and the kinked, irregular course it pursued (fig. 1).

b. Spindle-shaped bipolar cells

Spindle-shaped bipolar cells, unlike the tripolar cells, are not restricted in their distribution. In a body segment they may be found anywhere along the course of the three pairs of segmental nerves, i.e., at the margin of the cord itself, along the lateral nerve trunk, at the point of bifurcation of this trunk, along the dorsal and ventral portions of the nerve rings running between the two muscular layers, and in the peripheral nerves passing through the layer of circular muscles. Near the dorsal and ventral midbody region the bipolar cells are more often found in the peripheral branches. This of course would be expected since the nerve rings in this region are greatly reduced. Nearer the setae, however, the number of cells found in the nerve ring gradually increases and in the so-called intersetal tract small groups of cells, three, four, and five, are commonly found (fig. 2).

The spindle-shaped bipolar cells also exhibit some striking variations in size (figs. 3, 4). As already noted, von Szuts ('14) mentioned this as one of the characteristics by which he distinguished two types of cells, 'intermuskulären Nervenzellen' and 'intermuskulären sensorischen Ganglienzellen.' However, it does not seem possible to use this as a basis of classification, since a careful comparison of a large number of cells by means of camera lucida measurements shows that between the two extremes (figs. 3, 4) there is a nicely graded series of cells. Von Szuts ('14) also described a difference in the arrangement of the neurofibrils within the cells. He found that in the small cells, al-

though the neurofibrils might branch frequently, they never anastomose, while in each large cell a definite, dense network is conspicuous. In my preparations (silver nitrate), on the other hand, the difference in the arrangement of the neurofibrils, like the difference in size, does not appear to be at all important. Within all cells a definite network could be distinguished. (In studying the neurofibrillar arrangement within the cells a binocular mon-objective microscope, equipped with a substage condenser and an 1.8 fluorite immersion objective, was used.)

Moreover, the density of the network in different regions of individual cells was also found to vary. These differences in density seemed to be due to two factors: the presence of large 'vacuoles,' and the position of the nucleus. The significance of the 'vacuoles' is still a matter of conjecture (Kowalski, '09; Boule, '13), but in the region of a 'vacuole' (fig. 3) the network was usually sparse. The nuclei are spherical or ellipsoidal and with rare exceptions are eccentric in position, being nearer the proximal pole of the cell (figs. 2, 3, 4). The neurofibrillar network in the distal pole of the cell appears coarse and dense, but toward the proximal pole, in the vicinity of the nucleus, the density of the net is decreased and, as the cell narrows to give off its proximal process, the meshes of the net become elongated in the direction of the long axis of the cell (fig. 3).

The eccentric nuclei of the spindle-shaped bipolar cells give to these nerve elements a well-defined morphological polarity. Just what relation there is between the structure of these cells and the direction of conduction of impulses cannot be decided until some conclusion is reached regarding the nature of these cells; i.e., whether they are connected with the receptor or the effector portion of the nervous system. Kowalski ('09) points out that in the earthworm the neurofibrils which form an efferent ('cellulifuge') process are not united into a net, but converge without branching and fuse, giving rise to the single fiber; while on the other hand, the afferent ('cellulipete') process on entering the body of the cell is broken up into a number of branching and anastomosing neurofibrils. Boule ('13) criticises this view of Kowalski and figures the intermuscular nerve cells with anastomosing neurofibrils in both poles.

c. Crescent-shaped bipolar cells

Relatively few crescent-shaped bipolar cells were observed in the earthworm, but they were distinctly shown by both the methylene-blue and the silver-nitrate methods. All the cells observed were remarkably uniform in size and form. Their distribution, too, was decidedly limited, as all the examples noted were situated between the dorsal and ventral members of the several pairs of setae.

The cells lie in spaces in the outer portion of the circular muscle layer quite close to the epidermis (fig. 5). The poles of the cells (horns of the crescent) were directed outward and the processes leaving both poles also passed outward, becoming lost eventually in the basiepithelial network described by Dechant ('06) and others. I have been unable to find any mention of a cell of this type in the literature. Its significance will be discussed later.

d. Long, slender, pyramidal, or spindle-shaped cells

These cells are quite different from any already described and were successfully demonstrated by means of the methylene-blue-immersion method. The cells appeared only in preparations in which the sense organs of the epidermis were selectively stained, and in the use of methylene blue in this work it was generally found that if the cells of the ventral chain and the intermuscular tripolar and bipolar cells were brightly stained, the epidermal sense cells were very faintly stained, and vice versa. Long, slender pyramidal cells were never observed in silver-nitrate preparations. In this connection it should be added that the writer was unable, with the modification of Ramón y Cajal's method, to secure satisfactory impregnations of the epidermal sense organs. Kowalski ('09, figs. 47 to 50), however, following a similar procedure, did not apparently encounter this difficulty.

The staining characteristics noted above suggested at once that these deeper-lying cells might be similar in nature to the epidermal sensory cells, and both their position and the relation of their fibers to other tissues strengthen this idea. All the examples (eight) of the slender cells were found on the ventral side

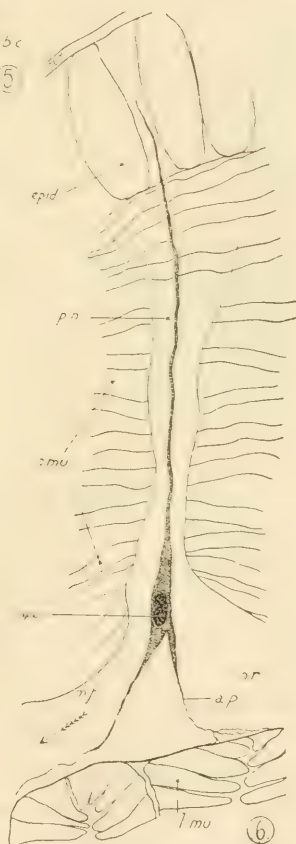
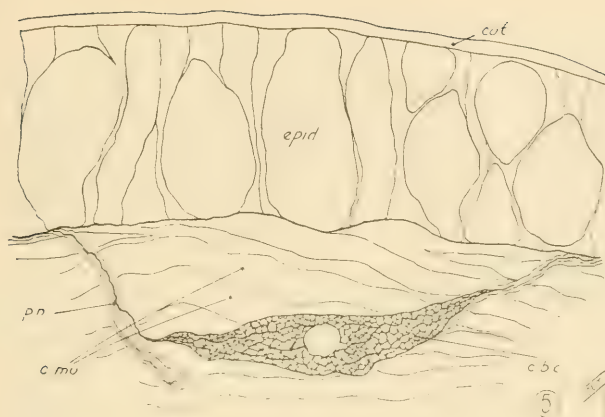


Fig. 5 Crescent-shaped bipolar cell lying within the layer of circular muscles and between the ventral pair of setae. *c.b.c.*, crescent-shaped bipolar cell; *c.mu.*, circular muscles; *cut.*, cuticula; *epid.*, epidermis; *p.n.*, peripheral nerve. Ramón y Cajal method modified. $\times 540$.

Fig. 6 Deep lying sensory cell on the ventral surface of the earthworm. *a.p.*, accessory process; *c.mu.*, circular muscles; *cut.*, cuticula; *epid.*, epidermis; *l.mu.*, longitudinal muscles; *m.f.*, main fiber; *n.r.*, nerve ring; *p.n.*, peripheral nerve; *s.p.c.*, pyramidal sensory cell. Immersion methylene-blue method. $\times 540$.

Fig. 7 A group of three cells from an epidermal sense organ. *a.p.*, accessory process; *b.e.n.*, basiepithelial net; *c.mu.*, circular muscles; *m.f.*, main fiber; *s.c.*, sense cells. Immersion methylene-blue method. $\times 540$.

of the earthworm. It is difficult to decide whether this is the normal distribution or whether only the cells in this position were stained, since the preparations were not obtained by intracoelomic injections, but by partially immersing the live animal in the staining solution. The dorsal portion of the animal accordingly was not in direct contact with the stain.

The bases of the cells were found to lie at the level of the nerve ring, while the long slender cell bodies extended outward through the muscle layer and pierced the epidermis (fig. 6). The intra-epidermal portion, lying between the columnar cells, was represented only by a very fine process which in no case could be positively traced further than one-half the way to the cuticular surface. One main fiber and one or two accessory fibers usually arose from the bases of the cells. The main fiber in one case was traced through five successive sections, each $20\ \mu$ thick. It was found to enter the lateral nerve trunk, to pass into the ventral nerve cord, and, branching slightly, to terminate on its own side in a dorsal position. The accessory processes could rarely be traced among the fibers of the nerve ring, but in one cell a short process was seen to branch slightly and end at the surface of the longitudinal muscle layer (fig. 6).

In general appearance and structure the slender nerve cells differ in several respects from the other intermuscular cells as seen in methylene-blue preparations, but exhibit several features which are strikingly like those observed in epidermal sense cells (figs. 6, 7). Their nuclei are oval or ellipsoidal, contain no well-defined nucleolus, and stain densely. Their bodies stain less heavily, but take the color uniformly. The other intermuscular nerve cells and the cells of the ventral cord, on the other hand, have spherical nuclei, delicate chromatin networks, definite nucleoli, and well-defined neurofibrillar networks.

SIGNIFICANCE OF THE INTERMUSCULAR NERVE CELLS

The question of the significance of the intermuscular nerve cells is a difficult one to discuss. Schneider ('02, p. 392) suggested that these scattered cells were possibly sensory in nature,

giving rise to some of the free terminations found within the epidermis. Kowalski ('09), in referring to the tripolar cells (he apparently did not observe those of the bipolar type), expressed his view as follows: "Ces cellules nerveuses profondes, origine peut-etre des terminaisons sensorielles libres intraepidermiques, permettent de rapprocher le système nerveux des Oligochètes de celui des Polychètes, des Cestodes, et des Mollusques." Dechant ('06), although he recognized both tripolar and bipolar cells in the nerve rings, did not express any definite view as to their significance. In commenting, however, on the theory of the origin of the dorsal spinal ganglion of vertebrates from epidermal sensory elements which have retreated from their superficial position in invertebrates, he states:

Es können demnach die Sinnesnervenzellen der Wirbellosen mit den Spinal-ganglienzellen der Wirbeltiere gar nicht verglichen werden, sondern höchstens die Ursprungselemente der freien Nervenendigungen der Wirbellosen mit den Spinalganglienzellen der Wirbeltiere. Da aber jene noch nicht gefunden sind, so ist ein weiterer Ausbau dieses Vergleiches und der strenge Nachweis seiner Richtigkeit der Zeit noch nicht möglich. Unsere nächste Aufgabe wird in der Erforschung jener uns noch unbekannten Zellen gegeben sein.

Dechant's chief objection to the phylogenetic theory was based on his belief that the free nerve endings in the epidermis represent just as primitive a condition as sensory epidermal cells. Von Szuts ('14), on the other hand, who recognized only the two types of bipolar cells, accepts the evolutionary principle and homologizes the intermuscular ganglion cells of the earthworm with the ganglion cells of the dorsal spinal ganglion and ganglion cells of the retina.

In an attempt to interpret the function and significance of the four types of cells which have been described in this paper, it seems best, since there is little in the way of experimental work which bears directly on this subject, to approach the problem from the evolutionary view-point. In the primitive nervous system, as seen in the Coelenterata, there is usually a receptive epidermal cell which is intimately united by its branching processes with a deeper-lying cell, the ganglion cell or motor cell,

which is in turn connected with the muscles or other effectors. In addition to this, the sensory cell and the motor cell may also be united with other ganglion cells of the nerve net, to provide for the diffusion of an impulse from any one point.

In the earthworm, although there is a well-defined central nervous system, there are still vestiges of the more primitive condition. It has been recognized for a long time that the epidermal sensory cells of this animal possess, beside their main fiber, several accessory processes (fig. 7) which extend into and apparently anastomose with the basiepithelial network. Extending from this network, according to Dechant ('06), there are many intercellular fibers which do not end freely in the epidermis at various levels as usually described, but which continue outward and end superficially just beneath the cuticula. They may even anastomose at this level. Definite pericellular nets have been described about the large unicellular glands and Dechant has also demonstrated a very complex nerve net in the region of the setae. In addition to these peripheral structures, there are the various nerve cells scattered through and between the muscular layers.

Both tripolar cells (Kowalski, '09) and bipolar cells (von Szuts, '14) have been interpreted as representing sensory cells retreating from a superficial position to give rise phylogenetically to the cells of the dorsal spinal ganglia of the vertebrates, and the intraepidermal fibers were believed to belong to these cells. However, in their structure and staining reactions, and in the appearance of their fibers (coarse and irregularly kinked), the tripolar and bipolar cells resemble very closely the motor and association neurones found within the ventral chain. Furthermore, the relation of the crescent-shaped bipolar cells between pairs of setae, with both processes extending into the basiepithelial net and with no fiber extending to the central system (fig. 5), argues strongly against any theory that these intermuscular cells are deep-lying sensory cells. From the evolutionary standpoint also it seems equally as logical to interpret them as scattered ganglion or motor cells of the primitive nerve net which have not yet been incorporated into the ventral nerve chain.

Indeed, the latter interpretation, for a number of reasons, appears the more probable. In the first place, there are the structural and staining resemblances between these cells and those of the ventral cord. In the second place, the position of the crescent-shaped, bipolar cells, the absence of any processes passing from them to the central system, and the relations of the cells to the basiepithelial nerve net are suggestive of a possible rôle in the correlation of the movements of pairs of setae. (The basiepithelial net is probably continuous with the net surrounding the setae, since the setae themselves have an epidermal origin.) A third reason, perhaps a stronger one than either of the foregoing, is that one finds spindle-shaped bipolar cells widely distributed along the nerve tracts from within the margin of the ventral chain to a position close to the epidermis. Finally, the varying positions of the tripolar cells and the varying relations of their processes to other parts of the metamere also suggest an associational rather than a receptor function.

The fourth type of cell described (fig. 6), however, appears to possess all the features characteristic of sensory cells, differing from the epidermal sensory cells mainly in their position and in the length of their peripheral processes (figs. 6, 7). In all other features, such as staining reactions, shape, nuclear structure, and the possession of both a main axone and one or more accessory fibers, the epidermal and deep-lying cells are essentially alike. Just what function these deep-lying sensory cells perform, it is difficult to surmise. Their position in the circular muscle layer and their possible restriction to the ventral region indicate a probable rôle in connection with the initiation or maintenance of the creeping movements of the worm.

If we accept the evidence in favor of regarding the bipolar and triangular tripolar cells as being concerned with a motor or associational function and not primarily part of the receptor system, we are necessarily required to attempt an explanation of the origin of the intracuticular nerve fibers. They are too numerous to belong to the deep-lying sensory cells described, since each of these so far as observed sends but one fine process into the epidermis. However, in the midbody region, on which this

study was made, the gland cells are predominant in the epidermis, and it does not appear necessary to regard the intraepidermal fibers as being part of the afferent system. They might, it seems with equal right, be regarded as part of the efferent system innervating the epidermal effectors, the unicellular slime glands.

SUMMARY

1. In the earthworm, scattered nerve cells, probably vestiges of the primitive nerve net of lower invertebrates, are found.

2. At least four morphologically distinct types of cells are present in certain intermuscular regions, i.e., in the circular nerve rings between the longitudinal and circular muscle layers, and in the peripheral nerves within the layer of circular muscles.

3. Of the four types of cells, three, the spindle-shaped and crescent-shaped bipolar cells and the triangular tripolar cells, are believed to be associated with the effector portion of the nervous system and to represent outlying cells which, in the phylogenetic development of the central nervous system, have not been incorporated in the ventral cord.

4. The fourth type, the long slender pyramidal or spindle-shaped cells, are contained almost entirely within the circular muscle layer, but also send fine processes into the epidermis. In structure, staining properties, and their relation to the ventral cord, they resemble the cells of the epidermal sense organs and have been interpreted as deep-lying sensory cells.

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Resumen por el autor, Albert Kuntz.
Escuela Médica de la Universidad de Saint Louis.

El desarrollo del sistema nervioso simpático en el hombre.

En el hombre, el simpático guarda con el sistema nervioso cerebroespinal la misma relación genética que en los vertebrados inferiores. Las células que producen las neuronas del simpático derivan de los ganglios cerebro-espinales y del tubo neural. Las células que entran a formar parte de la substancia primordial de los troncos del simpático y plexos prevertebrales avanzan periféricamente a lo largo de las raíces dorsales y ventrales de los nervios espinales. Las que dan lugar a los ganglios de los plexos del simpático en el vago avanzan periféricamente a lo largo de los nervios vagos. Los grandes ganglios del simpático de la región craneal, esto es, los ganglios ciliares, esfenopalatinos, óticos y submaxilares, reciben células que avanzan periféricamente a lo largo de los nervios que transportan mas tarde fibras preganglionares a cada ganglio de los mencionados, y a lo largo de las divisiones respectivas del nervio trigemino.

Translation by José F. Nonidez
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THE DEVELOPMENT OF THE SYMPATHETIC
NERVOUS SYSTEM IN MAN

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THIRTY-ONE FIGURES

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INTRODUCTION

The development of the sympathetic nervous system has long been one of the perennial problems in vertebrate embryology. The literature on this subject, representing the work of a large number of investigators, has become voluminous, but reveals no general agreement regarding some of the fundamental aspects of the problem. The majority of the more recent investigators agree in general regarding certain phases of the problem, but disagree regarding others. The major portion of the fundamental work recorded is based on embryos of the lower vertebrates. Some important contributions are based on embryos of a variety of mammals, but relatively few of the observations recorded were made on human embryos.

The present writer published the results of his earlier studies on the development of the sympathetic nervous system in a series of papers ('09-'11). The conclusions drawn from these studies regarding certain fundamental aspects of the problem, especially with reference to certain portions of the sympathetic system, differ widely from those of the earlier investigators. Some of these conclusions have been substantiated by the work of later investigators; some have suffered adverse criticism. More mature study on the part of the writer has fortified his confidence in the more fundamental conclusions, but has also revealed errors of major and minor importance both in observation and interpretation. In view of the present status of the problem, it has seemed desirable to undertake the present investigation in order to correct certain errors referred to above, to treat more adequately certain details of the problem which have not been adequately studied hitherto, and to secure more accurate and more extensive knowledge regarding the development of the sympathetic nervous system in the human species.

The observations recorded in this paper, except as otherwise indicated, were made on human embryos included in the Carnegie Embryological Collection. It is a real pleasure to express my indebtedness to Dr. G. L. Streeter for placing this collection at my disposal, for the opportunity of working in his laboratories, and for the technical assistance of members of his staff in the preparation of microphotographs.

REVIEW OF LITERATURE

The literature bearing on the development of the sympathetic¹ nervous system in vertebrates has been reviewed more or less fully by nearly all of the many investigators who have worked in this field. It was reviewed also by the present writer in 1910.

¹ The writer appreciates the need of a terminology applied to this division of the nervous system which could be accepted alike by anatomists and physiologists. However, inasmuch as the term 'sympathetic' was used in its broad sense by the writer in his earlier papers, as well as by the majority of the more recent investigators in this field, it seems advisable to use it in the same sense in this paper.

For the purposes of the present paper it will suffice to set forth the views which were prevalent at that time and to consider somewhat more fully the several papers which have appeared during the past decade.

While the great majority of the investigators in this field have agreed that the sympathetic is derived from the cerebrospinal nervous system, a few, of whom Camus ('12) is the most recent, have attributed to this division of the nervous system a mesodermal origin. Inasmuch as no purpose can be served at this time by discussing a theory which is so obviously erroneous, the work of the latter authors will not be considered further in this paper.

There has always been a divergence of opinion among the advocates of the ectodermal origin of the sympathetic nervous system regarding the exact sources and the histogenesis of the sympathetic cells. Ever since the genetic relationship of the sympathetic to the cerebrospinal nervous system was clearly pointed out by Balfour ('77), the majority of the investigators derived the cells which give rise to the primordia of the entire sympathetic nervous system from the cerebrospinal ganglia or the neural crest; however, there has been no general agreement regarding the method by which these cells are displaced from the cerebrospinal ganglia into the sympathetic primordia. According to the theory first set forth by Ónodi ('86), cells are forced to advance peripherally from the distal ends of the spinal ganglia by the pressure which is exerted by the newly formed elements back of them. These cells become displaced toward the dorsolateral aspects of the aorta and give rise to the primordia of the sympathetic trunks. His, Jr. ('91), introduced the principle of the active migration of the cells which give rise to the sympathetic primordia along the paths of the spinal nerves and the communicating rami. Some of the more recent investigators are of the opinion that migration of cells from the spinal ganglia occurs earlier than was observed by His, Jr., and that the majority of the cells which enter the primordia of the sympathetic trunks migrate through the mesenchymal tissue or in advance of the growing fibers of the spinal nerves and the com-

municating rami rather than along the compact fibrous paths of the latter.

The differences of opinion above set forth regarding the method by which cells which take part in the development of the sympathetic nervous system are displaced peripherally may be accounted for in part by fundamental differences in the morphogenesis of the sympathetic trunks in the several classes of vertebrates. The primordia of the sympathetic trunks arise in the Elasmobranchii as ganglionic enlargements on the spinal nerves (Balfour, '77; van Wijhe, '89; Hoffmann, '99). They arise in the Amphibia as aggregates of cells lying along the dorso-lateral aspects of the aorta after fibers are present in the communicating rami (Hoffmann, '02; Neumayer, '06). In birds the primary sympathetic trunks arise as a pair of cell-columns lying along the dorsolateral aspects of the aorta. These early give way to the secondary sympathetic trunks, the primordia of which arise as aggregates of cells just mesial to the ventral roots of the spinal nerves (His, Jr., '97). In mammals the primordia of the sympathetic trunks arise as cell-columns lying along the dorso-lateral aspects of the aorta (His, '90; Kohn, '05, '07). With these observed differences in the morphogenesis of the sympathetic trunks in mind, it is apparent that the theory advanced by Ónodi was based on his findings in the Elasmobranchii, while the theory of the active migration of cells into the sympathetic primordia was based primarily on observations made on embryos of birds and mammals.

A few investigators, notably Kohn ('05, '07) and Neumayer ('06), do not admit that active cell migration occurs, but account for the aggregates of cells which constitute the primordia of the sympathetic trunks by the proliferation of elements which are differentiated in situ in the spinal nerves. Obviously, the views of these authors are influenced by their allegiance to the theory of local differentiation and the multicellular nature of nerve-fibers.

Froriep, who like a number of investigators before him, had previously observed that cells of medullary origin advance peripherally along the ventral roots of the spinal nerves, in 1907 presented evidence which indicates that some of these cells enter

the primordia of the sympathetic trunks and expressed the opinion that it is essentially these cells which give rise to the neurones in the sympathetic nervous system. Cajal ('08) expressed essentially the same opinion. His observations on embryos of the chick led him to the conclusion that the sympathetic cells are true motor cells which are derived from the spinal cord.

The work of Froriep was attacked most vigorously by Held ('09) and Marcus ('09), both of whom adhere to the older theory, according to which the cerebrospinal ganglia (or the neural crest) constitute the sole source of the cells which enter the primordia of the sympathetic nervous system. Perhaps no one among the more recent investigators would concur in the opinion of Froriep and Cajal that all sympathetic neurones are derived from cells of medullary origin which advance peripherally along the fibers of the motor nerve roots; however, their conclusion that cells of this type enter the primordia of the sympathetic trunks has been amply confirmed.

The older investigators studied primarily the development of the sympathetic trunks and the sympathetic plexuses along the abdominal aorta. No extensive observations on the development of the sympathetic plexuses related to the vagi, viz., the pulmonary, the cardiac, and the enteric plexuses, were recorded prior to the publication of the earlier work of the present writer in 1909 and 1910; however, it was generally assumed that the cells which give rise to the neurones in these plexuses are derived from the primordia of the sympathetic trunks. The earlier work of Abel ('10) is in full accord with this general assumption. She derived the enteric plexuses in the chick from cells which migrate "from the spinal cord and the intervertebral ganglia downward through the mesentery to the gut." The later work of Abel will be referred to presently.

Observations on the development of the cranial portion of the sympathetic nervous system, except the ciliary ganglion, which were published prior to the beginning of the past decade are fragmentary and incomplete. The scattered literature bearing on the development of the ciliary ganglion was reviewed by Carpenter ('06). This review reveals a wide difference of opinion

regarding the exact sources and the histogenesis of this ganglion. According to Hoffmann ('85), Ewart ('90), and Chiarugi ('94, '97), it arises from cells which advance from the semilunar ganglion into the oculomotor nerve either directly or by way of the ophthalmic division of the trigeminal nerve. Dohrn ('91) expressed the opinion that in the Elasmobranchii the ciliary ganglion arises from cells which migrate from the midbrain along the path of the oculomotor nerve. Béraneck ('84), Reuter ('97), and Rex ('00) also derived this ganglion from cells present in the oculomotor nerve, but did not determine the exact sources of these cells. According to Carpenter ('06), the ciliary ganglion arises in the chick from cells which migrate from the wall of the midbrain along the oculomotor nerve, but later receives some cells which advance peripherally from the semilunar ganglion along the ophthalmic nerve. The available evidence bearing on the development of the other cranial sympathetic ganglia seemed to favor the assumption that the sphenopalatine, the otic, and the submaxillary are derived exclusively from the semilunar ganglion.

Such in brief was the status of the problem when the present writer initiated a series of studies on the development of the sympathetic nervous system in embryos of types of the several classes of vertebrates. The results of these studies which were published in a series of papers ('09-'14) indicate that the sympathetic bears essentially the same genetic relationship to the cerebrospinal nervous system throughout the vertebrate series. The sympathetic trunks, though differing somewhat in their morphogenesis in the several classes of vertebrates, arise from cells of cerebrospinal origin which advance peripherally both along the dorsal and ventral roots of the spinal nerves. The cells which give rise to the ganglia of the prevertebral plexuses are derived from the same sources. The sympathetic plexuses related to the vagi, viz., the pulmonary, the cardiac, and the enteric plexuses, except in the aboral portions of the digestive tube, are not genetically related to the sympathetic trunks, but arise from cells of cerebrospinal origin which advance peripherally along the paths of the vagi. This finding was corroborated by the work

of Abel ('12) on embryos of the chick and more recently by that of Stewart ('20) on embryos of the rat. The cranial sympathetic ganglia arise in a manner essentially analogous to that in which the sympathetic trunks arise. The ciliary ganglion arises in intimate association with the oculomotor nerve in all classes of vertebrates. The writer's observations on this ganglion agree with those of Carpenter ('06) which indicate that it arises from cells which advance peripherally both along the oculomotor and ophthalmic nerves. The conditions found to obtain in embryos of the lower vertebrates with respect to the other cranial sympathetic ganglia need not be set forth at this time. In embryos of the turtle and the chick the sphenopalatine ganglion was found to arise in the path of the great superficial petrosal nerve and to become connected early with the maxillary nerve. It receives cells which advance peripherally both along the great superficial petrosal and the maxillary nerves. In embryos of the pig the relationship of the primordium of this ganglion to the great superficial petrosal nerve was less obvious. While it was recognized that cells might enter this ganglion along the great superficial petrosal nerve, it was erroneously concluded that the sphenopalatine ganglion arises, in embryos of the pig, primarily from cells which advance peripherally from the semilunar ganglion. The writer's observations on the development of the otic ganglion led him to conclude that in embryos of the chick this ganglion arises primarily from cells which advance from the primordium of the superior cervical ganglion along the internal carotid nerve, while in embryos of the pig it arises almost exclusively from cells which advance peripherally along the mandibular division of the trigeminal nerve. In the light of the present investigation, these conclusions are obviously erroneous. They will be referred to again in a later section of this paper. The submaxillary ganglion is derived primarily from cells which advance from the semilunar ganglion along the path of the lingual division of the mandibular nerve.

In a recent series of papers Ganfini ('11-'18) has published extensive and detailed observations on the development of the sympathetic nervous system in embryos of types of all the classes

of vertebrates above the Elasmobranchii. According to his observations, the ganglia of the sympathetic trunks arise from 'neurocytes' which advance peripherally both along the dorsal and ventral roots of the spinal nerves. From the primordia of the sympathetic trunks cells advance farther ventrally and give rise to the ganglia in the plexuses along the abdominal aorta. The enteric plexuses, according to Ganfini, arise from cells derived from the primordia of the sympathetic trunks which advance farther ventrally and enter the walls of the digestive tube. He recognizes cells which advance distally along the vagi and enter the pulmonary, the cardiac, and the oesophageal plexuses, but he seems to be of the opinion that these cells migrate from the superior cervical ganglia. He also recognizes the double origin of the ciliary ganglion in the lower vertebrates. While he finds the contribution to this ganglion of cells which advance distally along the oculomotor nerve less obvious in mammalian embryos than in embryos of lower vertebrates, he does not exclude it even in embryos of this class of vertebrates; consequently, his conclusions regarding the development of the ciliary ganglion are in essential accord with those of Carpenter and the present writer. The sphenopalatine, the otic, and the submaxillary ganglia, according to Ganfini, are derived primarily from the semilunar ganglion.

The most recent work on the development of the cranial sympathetic ganglia is that of Stewart ('20) which is based on embryos of the rat. With respect to all these ganglia, except the ciliary, Stewart has adhered strictly to the theory that the cells which give rise to each respectively advance peripherally along the nerve, or nerves, which, in the adult, carry its preganglionic fibers. His findings will be considered further in a later section of this paper.

The scattered observations on the development of the sympathetic nervous system in human embryos which were published prior to 1910 were reviewed by Streeter ('12), who also recorded his observations. Further studies based on human embryos were published by Broman ('11). The work both of Streeter and Broman is in general accord with that of the earlier investi-

gators, according to whom the primordia of the entire sympathetic nervous system are derived from the cerebrospinal ganglia by the peripheral displacement of cells of neural-crest origin.

SYMPATHETIC TRUNKS

The primordia of the sympathetic trunks arise in human embryos about 5 mm. in length as small groups of cells lying along the dorsolateral aspects of the aorta in the lower thoracic and upper abdominal regions. These cells may be recognized among the mesenchymal cells by the slightly larger size and more intense staining reaction of their nuclei. In embryos 6 mm. in length (nos. 676, 242)² the sympathetic primordia are present from the lower cervical to the sacral region. By reason of the strong curvature of the embryo at this stage, the aggregates of cells constituting the primordia of the segmental ganglia lie in such close proximity with each other that the entire primordium of the sympathetic trunk appears as a continuous column of loosely aggregated cells. This condition obtains until the embryos have reached a length of 9 to 10 mm. and the primordia of the sympathetic trunks are present from the upper cervical to the sacral region. Longitudinal fibers may not be observed in the primordia of the sympathetic trunks until the segmental character of the latter has become apparent. In the upper thoracic and cervical regions the sympathetic primordia arise along the dorsal aspects of the descending aortae. Doubtless the position of these primordia is in part determined by the position of the great arterial trunks. Inasmuch as the paired descending aortae lie at an appreciable distance from the median plane and converge toward the unpaired dorsal aorta, the primordia of the sympathetic trunks lie farther from the median plane in the cervical and upper thoracic than in the abdominal region.

When the primordia of the sympathetic trunks first appear, the cells are very loosely aggregated and the fibers of the com-

² Numbers inserted in this manner are the serial numbers of human embryos in the Carnegie Embryological Collection.

municating rami cannot be traced among them. A little later the fibrous communicating rami may be traced into these cell aggregates (figs. 1 and 13). In the abdominal region some of these fibers tend ventrally along the lateral aspects of the aorta toward the regions in which the prevertebral plexuses arise (fig. 2). Cells of cerebrospinal origin are present, during early development, both in the dorsal and ventral roots of the spinal nerves as well as in the mixed nerve trunks and the paths of the communicating rami. Migrant cells of medullary origin associated with the fibers of the ventral root of a spinal nerve in an embryo 9 mm. in length are illustrated in figures 3A and 14. Such cells are present in the motor nerve roots both within and without the external limiting membrane and occasionally, as illustrated microphotographically in figure 14, *cvr*, an individual cell may be observed in the process of passing through this membrane. Beyond the junction of the dorsal and ventral roots of the spinal nerves the cells of medullary and ganglionic origin cannot be distinguished from each other. As these cells advance peripherally, some of them enter the sympathetic primordia to give rise to sympathetic neurones.

Some of the more recent investigators, including the present writer, have expressed the opinion that many of the cells which enter the sympathetic primordia migrate peripherally in advance of the growing nerve fibers. The early migration of sympathetic cells in human embryos was emphasized by Streeter ('12), who expressed the opinion that the majority of the cells which enter the primordia of the sympathetic trunks advance toward the aorta before fibers are present in the communicating rami; consequently, he described the early communicating rami as cellular strands. Ganfini ('17)³ also described cellular communicating rami in early mammalian embryos (guinea-pig and pig) which later give way to the fibrous rami. As is well known, the distal portions of growing nerve fibers are not brought out clearly by the ordinary staining processes; however, as illustrated in figures 1 and 13, fibers are present in the communicating rami relatively

³ I am indebted to my student, Mr. José Zozaya, for reading Ganfini's and other Italian papers.

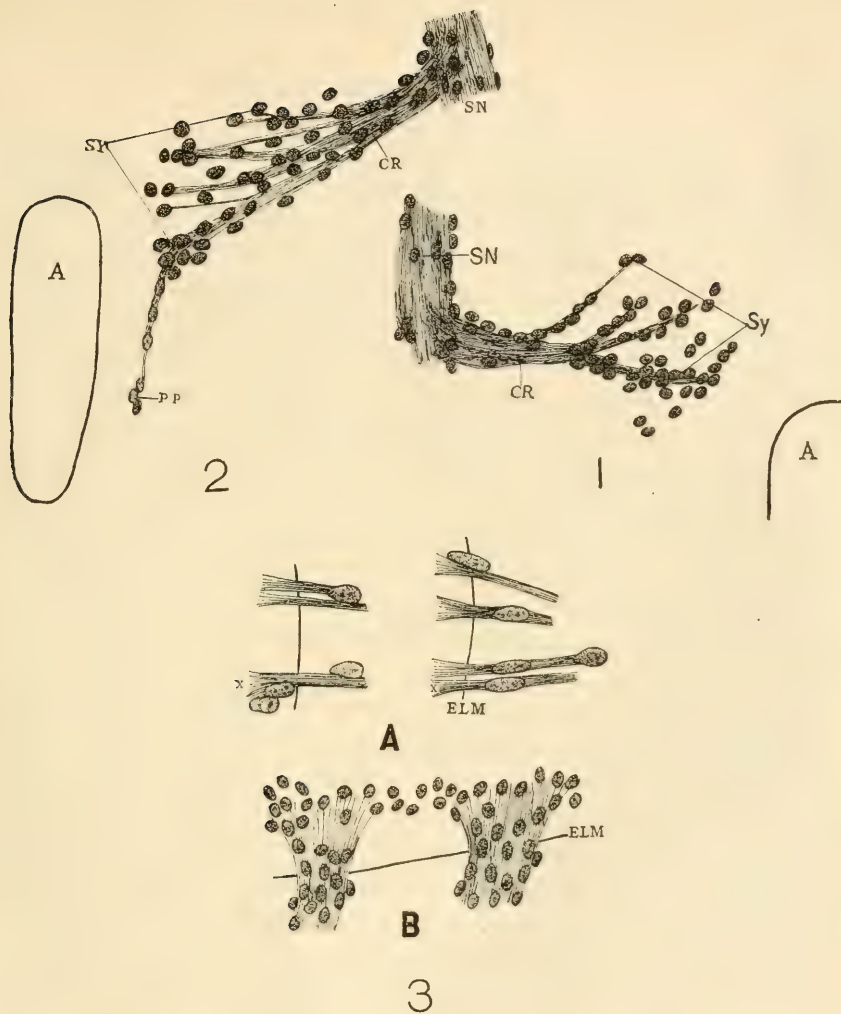


Fig. 1 Human embryo, 7 mm. in length, 617—13—1—3 \times 155.⁴ Transverse section through lower thoracic region showing spinal nerve and sympathetic trunk. To be compared with figure 13. A, aorta; CR, communicating ramus; SN, spinal nerve; Sy, sympathetic trunk.

Fig. 2 Human embryo, 6 mm. in length, 676—11—4—4. Transverse section through upper abdominal region showing spinal nerve and sympathetic trunk. A, aorta; CR, communicating ramus; PP, cells advancing into prevertebral plexus; SN, spinal nerve; SY, sympathetic trunk.

Fig. 3 A. Human embryo, 9 mm. in length, 721—12—3—4 and 5. Fiber-bundles with accompanying cells in ventral root of spinal nerve. B. Human embryo 11.5 mm. in length, 544—5—3—2. Vagus rootlets showing fibers with accompanying migrant cells. ELM, external limiting membrane; X, the same fiber bundle in successive sections

⁴ Numbers used in this manner indicate serial number of embryo, serial number of slide, row of sections on slide, number of section in row, and magnification.

early. Nevertheless, the writer is still of the opinion that the earliest cells enter the primordia of the sympathetic trunks in advance of the growing fibers.

That a fibrous tract is not essential for the peripheral migration of cells of cerebrospinal origin is obvious in embryos of the turtle in which, as observed by the writer in an earlier paper ('11), many of the cells which enter the primordia of the sympathetic trunks advance from the spinal nerves, not along the paths of the communicating rami, but directly through the mesenchyme. This observation was corroborated by Ganfini ('14) in embryos of other reptilian types. Obviously, if cells entering the sympathetic primordia could not be displaced in advance of the growing nerve fibers or in the absence of a fibrous path, the cells constituting the primordia of the sympathetic trunks would not occur as widely scattered in the mesenchyme as is the case even in human embryos.

The peripheral migration of cells of cerebrospinal origin into the primordia of the sympathetic trunks continues actively in human embryos for some time after the communicating rami have become fibrous. During the same interval the number of cells in these primordia is materially increased by local cell division. Human embryos 10 mm. and over in length afford little evidence that migration of cells along the communicating rami continues after a length of 12 mm. has been attained.

Relatively few careful observations on the development of the cervical portions of the sympathetic trunks have been recorded. All who made special mention of these structures in embryos of the higher vertebrates noted that their primordia arise later than the primordia of the thoracic portions of the sympathetic trunks. They also noted that there occurs a gradual extension of the cell-columns which constitute the primordia of the sympathetic trunks from the upper thoracic region cephalad until the level of the first cervical nerve is reached. Nevertheless, the general impression that each pair of cervical spinal nerves makes its contribution of cells to these primordia seems to prevail. Ganfini ('17) maintains that in early embryos both of the guinea-pig and the pig cellular communicating rami extend from

the cervical spinal nerves toward the primordia of the sympathetic trunks and that 'neurocytes' advance into the latter along these cellular rami. These cellular rami disappear early, according to Ganfini, after which there are no connections between the cervical spinal nerves, except the last, and the sympathetic trunks until the fibers which constitute the gray communicating rami are present. Although the writer has given especial attention to the development of the cervical portion of the sympathetic trunks, both in human embryos and in embryos of the pig, he was unable to substantiate this observation of Ganfini, nor could he obtain any evidence that the cervical spinal nerves with which no white communicating rami are associated play any part in the development of the sympathetic trunks. The writer's observations indicate that the primordia of the sympathetic trunks grow cephalad from the lower cervical region both by the displacement of cells along the dorsal aspect of the descending aortae and by local cell division. In this connection Streeter's observation that in the cervical and upper thoracic regions the primordia of the sympathetic trunks are not segmental, but "the cells remain massed in larger clumps, and these result in ganglia corresponding to from two to five segments," is not without interest. The cervical portions of the primordia of the sympathetic trunks are indeed continuous cell-columns until the condensations which result in the ganglia characteristic of the cervical sympathetic trunks are initiated.

In embryos 10 mm. in length the cell-masses constituting the primordia of the sympathetic trunks have become larger and more compact (fig. 16, *sy*). Although some of the cells still remain somewhat scattered, the segmental character of the sympathetic trunks is becoming more apparent and longitudinal fibers are present; however, the rami connecting the adjacent ganglia are nowhere free from sympathetic cells. As development advances the curvature of the embryo becomes less marked, and the ganglia of the sympathetic trunks become more widely separated. These ganglia also become more compact and more sharply delimited. In sagittal sections of an embryo 15 mm. in length (no. 390) the segmental character of the sympathetic trunks is well marked

throughout the thoracic and abdominal regions. The condensations which result in three ganglionic masses in the cervical region also have become apparent. Fibers may now be traced from the upper ends of the superior cervical ganglia cephalad along the internal carotid arteries. These ganglia are not sharply limited at their upper extremities, and apparently some cells advance along the fibers of the internal carotid nerves. The majority of these cells probably become incorporated in the plexuses on the internal carotid arteries. In embryos 20 to 22 mm. in length the sympathetic trunks have assumed a relationship to the vertebral condensations. The ganglia are quite sharply delimited and the fibrous rami between them are relatively free from cells.

PREVERTEBRAL PLEXUSES

In the upper abdominal region of an embryo 6 mm. in length (no. 676) a few cells may be traced from the primordia of the sympathetic trunks ventrally along the lateral aspects of the aorta. In a few segments of this embryo and in embryos which are somewhat farther advanced some of the fibers of the communicating rami tend ventrally along the paths of these cells (fig. 2). In embryos which are somewhat older, fibers which arise from cells in the primordia of the sympathetic trunks also grow ventrally into the region in which the ganglia of the prevertebral plexuses arise. During this interval cells become separated from the ventral borders of the primordia of the sympathetic trunks throughout the abdominal region and advance ventrally to give rise to the ganglia of the prevertebral plexuses. At the same time other cells which are associated with those fibers of the communicating rami which turn ventrally without passing through the ganglionic masses at the dorsolateral aspects of the aorta advance into the prevertebral plexuses more or less directly from the spinal nerves. In embryos 9 to 10 mm. in length the aggregates of sympathetic cells lying along the ventral and ventrolateral aspects of the abdominal aorta have assumed considerable size. In an embryo 10.1 mm. in length (no. 623) these

cell-masses are very conspicuous all along the abdominal aorta (figs. 16 and 17, *pv*). At this stage some cells have already become displaced laterally from these masses toward the primordia of the adrenal glands and along the renal arteries. The greatest accumulation of sympathetic cells ventral to the abdominal aorta occurs about the coeliac artery. The several plexuses which arise along the abdominal aorta are not yet clearly delimited. Neither can fibers be traced from these plexuses into the mesentery. As development advances these several plexuses become more clearly differentiated, while the ganglionic masses become relatively larger and more compact. From these ganglionic masses cells may be traced into the adrenal glands as well as along the renal and spermatic (or ovarian) arteries.

VAGAL SYMPATHETIC PLEXUSES

The writer has presented evidence in the series of earlier papers referred to above which shows clearly that throughout the entire vertebrate series the pulmonary, the cardiac, and the enteric plexuses, except in the aboral portions of the digestive tube, are not genetically related to the sympathetic trunks, but arise from cells of cerebrospinal origin which advance peripherally along the paths of the vagus nerves. These findings were first substantiated by Abel ('12) in embryos of the chick. Abel ('10) had previously derived the enteric plexuses in the chick exclusively from cells which migrate "from the spinal cord and the intervertebral ganglia." Following the publication of the writer's earlier papers, she undertook a reinvestigation of the development of the sympathetic nervous system in the chick. In this work she employed specialized methods and studied the development of the sympathetic plexuses related to the vagi in considerable detail. Her findings regarding the development of the pulmonary, the cardiac, and the enteric plexuses agree in all essential respects with the results of the work of the present writer which had previously been published. Recently Stewart ('20) has presented evidence based on embryos of the rat which he interprets as indicating "that part if not all of the nerve cells found in the

cardiac, gastric, tracheal, oesophageal, pulmonary, and upper intestinal plexuses are of vagus origin."

The present series of observations on human embryos agree, with regard to the genetic relationship of the pulmonary, the cardiac, and the enteric plexuses to the vagus nerves, with the earlier observations of the writer on embryos of other vertebrates. In human embryos 5 mm. in length, in which the primordia of the sympathetic trunks are present only in the thoracic and upper abdominal regions, the vagus nerves may be traced distally somewhat beyond the bifurcation of the trachea. Branches of the vagi bearing small accumulations of cells of nervous origin come into close proximity with the oesophageal wall. In embryos of this stage as well as in embryos which are somewhat farther advanced the vagus nerves have the appearance characteristic of nerve trunks along which cells of cerebrospinal origin migrate peripherally. In favorable sections continuous lines of cells of medullary origin may be observed extending into the vagus rootlets (fig. 3, *B*), indicating an active migratory process. In sagittal sections the ganglia on the vagus trunks appear as large oval or elliptical cell-masses which are not sharply limited distally. Furthermore, cells identical in appearance with those present in the ganglionic masses are present in abundance in the nerve trunks as far as the latter may be traced. These cells are identical in appearance also with those which migrate peripherally along the spinal nerves and the communicating rami.

In embryos 6 mm. in length (nos. 241 and 676) branches of the vagi may be traced distally as far as the cardiac region of the stomach and for a short distance along its lesser curvature. Wherever vagus fibers occur in these embryos they are accompanied by cells of nervous origin, many of which occur in small aggregates. The primordia of the oesophageal plexuses may be recognized at this stage. Vagus fibers accompanied by cells of nervous origin may also be traced along the bronchi toward the roots of the lungs. In embryos 7 to 9 mm. in length all of these nervous complexuses have become better developed, the cell-aggregates also have become more numerous and many of them are larger. In sagittal sections of an embryo 9 mm. in length a

distinct vagus branch accompanied by migrant cells may be traced into proximity with the bulbar region of the heart. This nerve gradually becomes larger and cells become aggregated near its distal end. In an embryo 14 mm. in length (no. 511) it shows a considerable accumulation of these migrant cells near its distal extremity, as illustrated in the accompanying figure (fig. 4) which is taken from the microphotograph of a sagittal section shown in figure 15. This mass of cells constitutes a portion of the primordium of the cardiac plexus. Over the dorsal aspect of the heart the plexiform network around the oesophagus comes into very close proximity with the atrial walls. In transverse sections of an embryo 10.1 mm. in length (no. 623) the oesophageal plexus is very conspicuous (figs. 5, 18, and 19). The branches of the vagi with their accompanying cell-aggregates form a plexiform network including many cell-masses which is somewhat richer over the dorsal and lateral aspects of the oesophagus than between the latter and the trachea. Below the bifurcation of the trachea, vagus fibers accompanied by cells of cerebrospinal origin may be traced into the roots of the lungs where masses of cells of the same type occur in proximity with the bronchi and the pulmonary vessels (figs. 6, *pp*, and 20, *pp*). These plexiform networks which constitute the primordia of the pulmonary plexuses are continuous with the oesophageal plexus as well as with that portion of the cardiac plexus which is associated with the atrial walls.

In the writer's preparations of embryos of the pig 6 to 12 mm. in length the oesophageal plexus is less conspicuous than in human embryos of corresponding stages; however, vagus branches accompanied by migrant cells of nervous origin are present in considerable abundance around the oesophagus. By reason of the proximity of many of these elements with the oesophageal epithelium, they were erroneously interpreted as representing mainly the primordia of the enteric plexuses. The same error in interpretation, though it is less apparent, occurs also in the writer's studies of the development of the sympathetic nervous system in the other classes of vertebrates. The primordia of the oesophageal plexus are present before either nerve cells or fibers

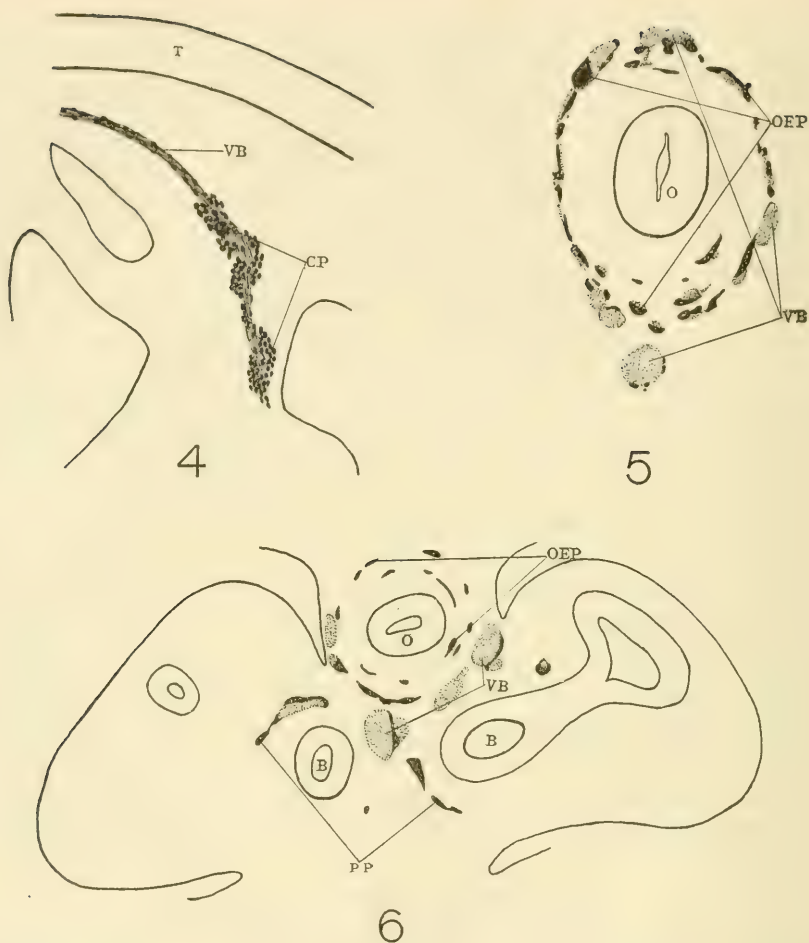


Fig. 4 Human embryo, 14 mm. in length, 511—9—1—2×80. Sagittal section showing trachea and upper portion of heart. To be compared with figure 15. CP, portion of cardiac plexus; T, trachea; VB, vagus branch to heart.

Fig. 5 Human embryo, 10.1 mm. in length, 623—13—2—2×120. Oesophageal plexus in transverse section. To be compared with figure 19. OEP, cell-masses in oesophageal plexus; O, oesophagus; VB, vagus branches.

Fig. 6 Human embryo, 10.1 mm. in length, 623—11—2—4. Transverse section through lungs. To be compared with figure 20. B, bronchus; O, oesophagus; OEP, cell-masses in oesophageal plexus; PP, cell-masses in pulmonary plexuses; VB, vagus branches.

occur within that portion of the mesenchyme which becomes differentiated into the muscular and submucous layers of the oesophageal wall. Nevertheless, some nerve cells which become incorporated in the enteric plexuses penetrate into this mesenchymal tissue very early, although they do not show a definite concentric arrangement until somewhat later. Such cells are present in considerable abundance, especially at the lower levels of the oesophagus in human embryos 7 to 9 mm. in length. Doubtless, the above error in interpretation is in large measure responsible for the discrepancy which Stewart ('20) has emphasized between his observations on this nervous complex in embryos of the rat and those of the present writer in embryos of the pig.

In embryos 10 mm. in length vagus branches accompanied by migrant cells are present all along the lesser curvature of the stomach in the mesenchymal tissue which is becoming differentiated to form the wall of that organ. During the succeeding stages of development vagus branches spread round the stomach and extend farther distally along the intestine. The cells which give rise to the enteric plexuses increase in number, and as the muscular and submucous layers of the wall of the digestive tube become differentiated, these minute ganglionic cell-masses become concentrically arranged in two layers which give rise to the myenteric and submucous plexuses.

It is important to note that no paths along which cells migrate from the sympathetic trunks or the prevertebral plexuses into the pulmonary, the cardiac, and the enteric plexuses in the more proximal portions of the digestive tube are established during the early stages of development. Indeed, the latter plexuses develop simultaneously with the sympathetic trunks and the prevertebral plexuses. Sympathetic nerves grow into the plexuses related to the vagi somewhat later, but not until the great majority of the cells which enter their primordia are already present. Although the possibility that some cells may be added to these plexuses after fibrous connections with the sympathetic trunks are established is not precluded, we must conclude that they arise primarily from cells of cerebrospinal origin which advance peripherally along the vagi.

To what extent cells which advance peripherally along the vagi take part in the development of the enteric plexuses in the more distal portions of the intestine is not clear. The evidence at hand favors the conclusion that the primordia of these plexuses gradually extend distally from the upper levels of the intestine in which the cells are certainly derived from the vagus supply. On the other hand, the lower portions of the intestine, especially the large intestine, arises in close proximity with the prevertebral plexuses in the lower abdominal and pelvic regions. Paths along which sympathetic cells may migrate from these plexuses into the walls of the intestine are established relatively early. Obviously, the enteric plexuses in the lower portions of the intestine are derived from the sympathetic supply in the lower trunk region.

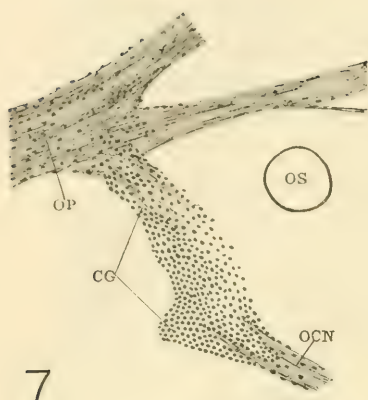
CRANIAL SYMPATHETIC GANGLIA

Ciliary ganglion

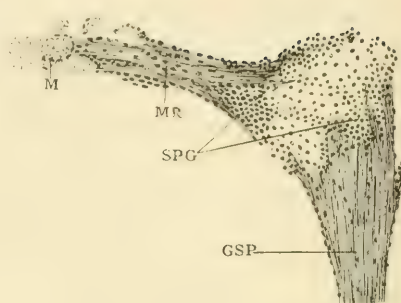
Doubtless the ciliary ganglion represents the most primitive of the well-defined sympathetic ganglia in the cranial region in the higher vertebrates. Its development has been studied in embryos of types of all the classes of vertebrates. The majority of the more recent investigators, including the present writer, have agreed that this ganglion arises from cells of cerebrospinal origin which advance peripherally both along the oculomotor and ophthalmic nerves. However, both Broman ('11) and Streeter ('12) failed to recognize cells which advance peripherally along the oculomotor nerve and enter the primordium of the ciliary ganglion in human embryos. They derived the ciliary exclusively from the semilunar ganglion. Ganfini ('17) pointed out that the contribution of cells from the oculomotor nerve to the ciliary ganglion is much less obvious in mammalian embryos (guinea-pig and pig) than in embryos of types of other classes of vertebrates; however, inasmuch as its double origin is clearly established in other classes of vertebrates, he concluded that this ganglion is genetically related both to the oculomotor and ophthalmic nerves also in mammals. Although Stewart ('20) maintains that all the other cranial sympathetic ganglia arise exclusively from cells

which advance peripherally along the nerves which carry the preganglionic fibers to each respectively, he found no evidence in embryos of the rat that any of the cells which become incorporated in the ciliary ganglion advance peripherally along the oculomotor nerve.

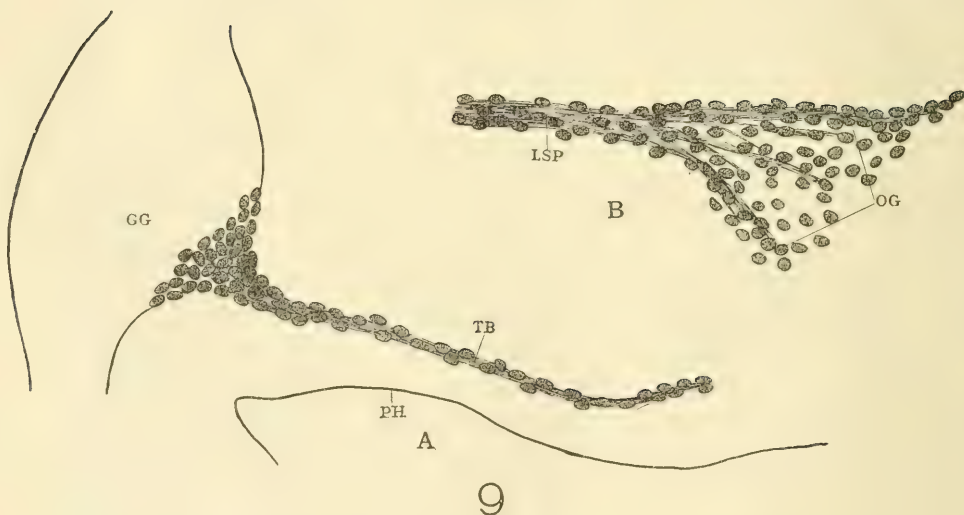
The migration of cells along the oculomotor nerve in early human embryos is not very apparent; however, in a number of instances an aggregate of intensely staining cells was observed on the oculomotor nerve trunk at the level at which the ciliary ganglion arises before cells could be traced thither from the ophthalmic nerve. Doubtless, these cells become incorporated in the ciliary ganglion. The ophthalmic nerve in early human embryos has the appearance of a path along which active migration of cells is taking place. Continuous lines of cells extend from the semilunar ganglion along this nerve trunk. Migrant ganglion cells become aggregated very early at a point just proximal to the origin of the nasociliary ramus. As this aggregate of cells grows larger, it advances toward the oculomotor nerve until it makes intimate contact with the latter at the point at which the aggregate of cells noted above is located. When this is accomplished the primordium of the ciliary ganglion consists of a continuous mass of cells extending from the ophthalmic to the oculomotor nerve. This condition, as it appears in sagittal sections of an embryo 14 mm. in length, is illustrated in the accompanying figure (fig. 7) which is taken from the microphotograph in figure 21. Nerve fibers may be traced from the ophthalmic nerve into the primordium of the ciliary ganglion at this stage, but they are largely obscured by the densely aggregated cells. As development advances this ganglionic mass becomes somewhat removed from the ophthalmic nerve trunk, but remains in intimate contact with the oculomotor nerve until relatively late. As compared with the total number of cells comprised in the primordium of the ciliary ganglion in human embryos, the small group of cells which becomes aggregated early on the oculomotor nerve is relatively unimportant. Nevertheless, the evidence warrants the conclusion that in human embryos, as in the embryos of other vertebrates, the ciliary ganglion is genetically related both to the ophthalmic and the oculomotor nerve.



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Fig. 7 Human embryo, 14 mm. in length, 511-12-2-2 \times 80. Sagittal section through ciliary ganglion. To be compared with figure 21. *CG*, ciliary ganglion; *OCN*, oculomotor nerve; *OP*, ophthalmic nerve; *OS*, optic stalk.

Fig. 8 Human embryo, 20 mm. in length, 462-15-1-1 \times 80. Section showing sphenopalatine ganglion with maxillary ramus and nerve of the pterygoid canal entering it. To be compared with figure 25. *GSP*, nerve of the pterygoid canal; *M*, maxillary nerve; *MR*, maxillary ramus to sphenopalatine ganglion; *SPG*, sphenopalatine ganglion.

Fig. 9 A. Human embryo, 7.85 mm. in length, 1354-5-3. Sagittal section showing geniculate ganglion (*GG*) and tympanic nerve (*TP*). *PH*, posterior wall of pharynx. B. Human embryo 14 mm. in length, 411-4-2-1. Sagittal section showing otic ganglion (*OG*) and lesser superficial petrosal nerve (*LSP*).

Sphenopalatine ganglion

The primordium of the sphenopalatine ganglion arises at the growing tip of the greater superficial petrosal nerve as an aggregate of cells which advance from the geniculate ganglion along the path of this nerve. The earliest human embryos in which it was observed are 11 mm. in length (nos. 619 and 1836). The geniculate ganglion is not sharply limited during early development, but cells advance from its distal border along the fibers of the great superficial petrosal nerve. Cells of this type are present throughout the entire length of this nerve; consequently, it presents, during these early stages, the appearance characteristic of a slender nerve trunk along which cells of cerebrospinal origin advance peripherally.

This primordium of the sphenopalatine ganglion lies medial to, but not in contact with the maxillary nerve. This nerve is composed of numerous loosely aggregated bundles of fibers. Cells become separated from the semilunar ganglion and advance peripherally along these fiber bundles either singly or in small aggregates. In embryos 12 to 15 mm. in length rami deviate from the maxillary nerve near its origin from the semilunar ganglion and grow into the primordium of the sphenopalatine ganglion. Cells of ganglionic origin advance along these rami and become aggregated at their growing tips. This condition, as it appears in coronal sections of an embryo 14.6 mm. in length (no. 1919), is illustrated in figure 23. Sections which cut the maxillary nerve approximately at right angles at the level of the sphenopalatine ganglion in embryos 15 mm. and over in length show a fibrous ramus accompanied by numerous cells of nervous origin which extends from the maxillary nerve into the primordium of this ganglion. The same condition still obtains in embryos 20 and 21 mm. in length (nos. 462 and 460). Figures 8, 24, 25, and 26 are taken from sections of these embryos which show both a maxillary ramus and the nerve of the pterygoid canal, which comprises the fibers of the greater superficial petrosal nerve, growing into the primordium of the sphenopalatine ganglion. They show clearly that numerous migrant cells are still present along the

maxillary ramus, while the nerve of the pterygoid canal is relatively free from cells. Obviously, migration of cells into the sphenopalatine ganglion continues longer from the semilunar than from the geniculate ganglion. That the cells associated with the rami of the maxillary nerve which enter the sphenopalatine ganglion are at least in part cells which become differentiated into neurones is evidenced by the fact that in embryos 20 mm. and over in length many of them may be recognized as neuroblasts. Furthermore, as observed by Macklin,⁵ ganglionic masses of neuroblasts occur on these rami or at their origin from the maxillary nerve in embryos 40 mm. and over in length. The deep petrosal joins the greater superficial petrosal nerve before migration of cells along the fibers of the latter ceases; however, there is no clear evidence that cells which accompany the fibers of the deep petrosal nerve enter the sphenopalatine ganglion.

The observations here set forth justify the conclusion that in human embryos the sphenopalatine ganglion arises in part from cells which advance from the geniculate ganglion along the greater superficial petrosal nerve and in part from cells which advance from the semilunar ganglion along the maxillary nerve and its rami. Obviously, the contribution of cells from the latter source is greater than that from the former. The writer's earlier observations on the development of the sphenopalatine ganglion in embryos of the pig ('13) led him to the conclusion that this ganglion arises primarily from cells which advance from the semilunar ganglion along the maxillary nerve and its rami, and that it receives relatively few cells from the geniculate ganglion via the greater superficial petrosal nerve. A reinvestigation of the development of this ganglion in embryos of the pig has convinced the writer that he failed in his earlier work to recognize the greater superficial petrosal nerve as a migration path until cells could already be traced from the semilunar ganglion into the primordium of the sphenopalatine ganglion. In embryos of the pig, as in human embryos, the earliest cells which enter the primordium of the sphenopalatine ganglion advance peripherally along the greater superficial petrosal nerve. Nevertheless, the

⁵ Unpublished communication.

majority of the cells which enter the primordium of this ganglion are derived from the semilunar ganglion along the maxillary nerve and its rami.

The recent work of Ganfini ('17) shows clearly that the majority of the cells which enter the primordium of the sphenopalatine ganglion in mammalian embryos (guinea-pig and pig) advance from the semilunar ganglion along the maxillary nerve and its rami. His description of the earliest maxillary rami entering the primordium of the sphenopalatine ganglion as bundles of fibers which deviate from the maxillary nerve near its origin from the semilunar ganglion is in full accord with the conditions in human embryos described above and illustrated microphotographically in figure 23. Ganfini does not consider the cells which may enter the sphenopalatine ganglion via the greater superficial petrosal nerve of any considerable importance in its development.

Stewart ('20) maintains that both in embryos of the pig and the rat the sphenopalatine ganglion arises exclusively from cells which advance from the geniculate ganglion along the greater superficial petrosal nerve. In the light of the observations on human embryos set forth above as well as the work of Broman ('11) and Streeter ('12) on human embryos and that of Ganfini ('17) on embryos of other mammalian types, the contribution of cells from the semilunar to the primordium of the sphenopalatine ganglion seems to be so clearly demonstrated that it does not seem advisable at this time to discuss the evidence bearing on this point any further.

Otic ganglion

The primordium of the otic ganglion arises in human embryos as an accumulation of cells at the growing extremity of the lesser superficial petrosal nerve. In embryos 7 to 8 mm. in length the tympanic branch of the glossopharyngeal nerve may be traced from the petrosal ganglion along the dorsal aspect of the pharynx as a slender ramus with which are associated numerous cells which are identical with those in the petrosal ganglion. Cells apparently advance from the petrosal ganglion into this ramus and migrate along its course. In sagittal sections of an embryo 7.85 mm. in length (no. 1354) this ramus may be traced from the petrosal ganglion nearly to the level of the geniculate ganglion. There are no marked accumulations of cells along its course, but

the entire ramus, as illustrated in the accompanying figure (fig. 9 A), contains numerous cells of nervous origin and presents the appearance of an early migration path. In embryos 10 mm. in length the tympanic nerve has been joined by fibers from the geniculate ganglion. The lesser superficial petrosal nerve may now be traced to a point a little below the level of the semilunar ganglion where a small mass of cells has become aggregated. In an embryo 14 mm. in length (no. 511) this mass has become somewhat larger, but the cells are still loosely aggregated. In sagittal sections of this embryo, as illustrated in figure 9 B, it is irregularly triangular and its upper angle comes into very close proximity with the semilunar ganglion. In sections of an embryo 13 mm. in length (no. 485), as illustrated microphotographically in figure 22, there is apparent cellular continuity between the primordium of the otic ganglion and the semilunar ganglion. This connection could not be observed in all embryos in approximately the same phase of development. In embryos 14 mm. and over in length the primordium of the otic ganglion lies in intimate contact with the mandibular division of the trigeminal nerve. This nerve, like the other divisions of the trigeminal, contains numerous cells of cerebrospinal origin which apparently advance distally along its course. Many of these cells are derived from the semilunar ganglion, others probably advance from the rhombencephalon along the motor root of the trigeminal nerve. Even in relatively late stages, as illustrated in figure 30 which is taken from a section of an embryo 14.5 mm. in length (no. 1267) continuous rows of cells may be traced from the rhombencephalic wall into the motor root of the trigeminal nerve. Doubtless, many of these cells advance peripherally along the motor fibers of the mandibular nerve. Fibrous rami may now be traced from the mandibular nerve into the otic ganglion. These rami, like the rami of the maxillary nerve which enter the sphenopalatine ganglion, are accompanied by migrant cells, some of which apparently advance into the otic ganglion. This condition obtains during a considerable interval. In embryos 20 and 21 mm. in length (nos. 460 and 462), as illustrated in figures 10, 27 and 28, the rami of the mandibular nerve leading into the otic ganglion

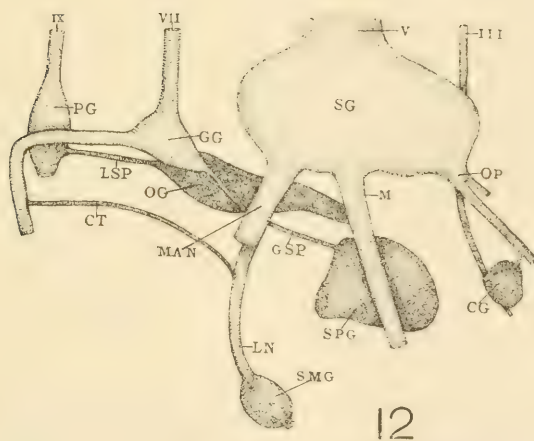
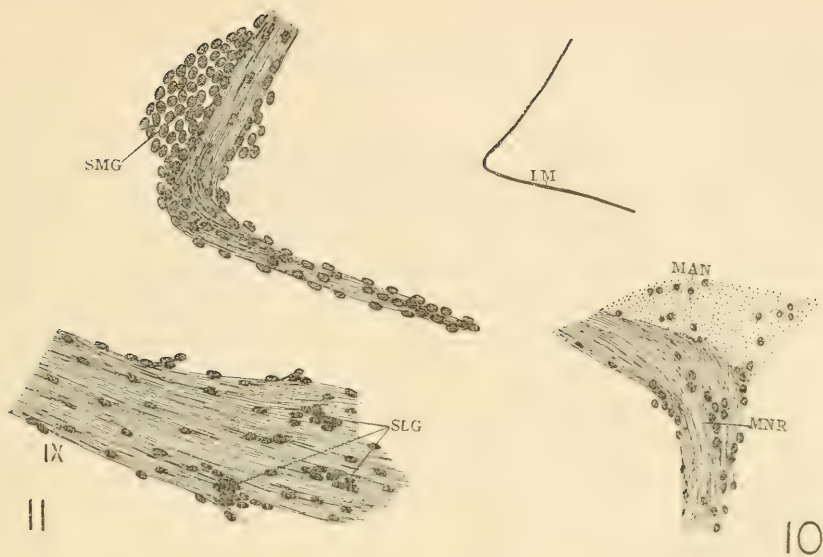


Fig. 10 Human embryo, 20 mm. in length, 462—14—2—3×165. Section through mandibular nerve and ramus to otic ganglion. To be compared with figure 27. *MAN*, mandibular nerve; *MNR*, mandibular ramus to otic ganglion.

Fig. 11 Human embryo, 14mm. in length, 940—14—2—3×160. Section through tongue. *IX*, lingual ramus of glossopharyngeal nerve; *LM*, margin of tongue; *SMG*, submaxillary ganglion; *SLG*, ganglionic masses associated with glossopharyngeal nerve.

Fig. 12 Diagrammatic reconstruction of the larger cranial sympathetic ganglia and the nerves to which they are genetically related in an embryo about 20 mm. in length. *CG*, ciliary ganglion; *CT*, chorda tympani; *GG*, geniculate ganglion; *GSP*, greater superficial petrosal nerve; *LN*, lingual nerve; *LSP*, lesser superficial petrosal nerve; *M*, maxillary nerve; *MAN*, mandibular nerve; *OG*, otic ganglion; *OP*, ophthalmic nerve; *PG*, petrosal ganglion; *SG*, semilunar ganglion; *SMG*, submaxillary ganglion; *SPG*, sphenopalatine ganglion.

still contains small aggregates of ganglion cells. Migrant cells are always more numerous at the periphery than in the interior of the larger nerve trunks. Inasmuch as the otic ganglion lies in immediate contact with the mandibular nerve, many of the cells advancing distally at the periphery of this nerve doubtless become incorporated in the ganglion. At any rate, a contribution of cells from the mandibular nerve to the otic ganglion cannot be precluded. Indeed, the majority of the cells which enter the otic ganglion probably come from this source. As in the case of the sphenopalatine ganglion, it may be observed that migration of cells into the otic ganglion continues later along the trigeminal fibers than along the other contributing path. Therefore, we are forced to conclude that, while the early primordium of the otic ganglion arises at the growing extremity of the lesser superficial petrosal nerve primarily from cells which advance from the petrosal ganglion, the majority of the cells which enter this ganglion are derived from the semilunar ganglion and the motor root of the trigeminal nerve.

In embryos 14 mm. and over in length the otic and sphenopalatine ganglia are connected with each other by a cellular strand (fig. 29). This cellular connection was observed in embryos up to 21 mm. in length, but not in later stages. It probably undergoes retrogressive changes during later development. The significance of this connection, if it has any, could not be determined.

The writer's earlier observations on the development of the otic ganglion in embryos of the pig led him to conclude that this ganglion arises primarily from cells of trigeminal origin. Further observations on early pig embryos have convinced him that he failed in his earlier work to recognize the lesser superficial petrosal nerve as a path along which cells advance into the otic ganglion until the period of most active migration along this path had elapsed. In embryos of the pig, as in human embryos, the first cells which enter the primordium of the otic ganglion advance peripherally along the lesser superficial petrosal nerve primarily from the petrosal ganglion, while the majority of the cells which enter this ganglion advance peripherally along the mandibular nerve and its rami.

The writer desires at this time to call attention to an error in his earlier work on the development of the otic ganglion in embryos of the chick ('14). In this instance the tympanic nerve was not recognized as a path along which cells migrate cephalad from the petrosal ganglion. The fibrous ramus which emerges from the plexuses on the internal carotid artery to join the tympanic nerve in the formation of the lesser superficial petrosal nerve is relatively large in embryos of the chick and shows some migrant cells. Having no sagittal sections of the earlier stages at hand, it was erroneously concluded that the majority of the cells which enter the otic ganglion advance from the plexus on the internal carotid artery. The writer is now of the opinion that relatively few if any cells reach the otic ganglion from this source, but that in embryos of the chick, as in mammalian embryos, the cells which enter the otic ganglion from other than trigeminal sources advance along the lesser superficial petrosal nerve primarily from the petrosal ganglion. A contribution of cells to the otic ganglion from trigeminal sources is less obvious in embryos of the chick than in mammalian embryos. Nevertheless, in the light of comparative studies, it cannot be excluded.

Broman('11) and Streeter ('12), who studied the development of the otic ganglion in human embryos, and Ganfani ('17), who employed embryos of other mammalian types (guinea-pig and pig), concur in the opinion that this ganglion is derived exclusively from the semilunar ganglion. On the other hand, Stewart ('20), basing his conclusions on observations made on embryos of the pig and the rat, maintains that the otic ganglion arises exclusively from cells which advance peripherally along the lesser superficial petrosal nerve.

Submaxillary ganglion

The primordium of the submaxillary ganglion arises relatively early in human embryos as an accumulation of cells in the path of the lingual division of the mandibular nerve. In embryos 10 to 11 mm. in length in which only the merest traces of the primordia of the sphenopalatine and otic ganglia are present the primordium of the submaxillary ganglion has already attained

considerable size. In view of the double origin of the other sympathetic ganglia associated with the trigeminal nerve, we should expect that both cells of trigeminal and of facial origin should take part in the development of the submaxillary ganglion. The writer could not, in embryos 10 to 11 mm. in length, trace the chorda tympani to its junction with the lingual nerve. Neither did he succeed in determining the exact phase of development in which this junction is effected. However, in view of the condition of the other rami of the facial nerve, especially the greater superficial petrosal nerve, in embryos in which the earliest traces of the submaxillary ganglion appear, it is safe to conclude that cells are aggregated in the path of the lingual nerve before the junction of the chorda tympani with the latter is effected. Therefore, the further conclusion that the earliest cells which enter the primordium of the submaxillary ganglion are cells of trigeminal origin is also justified. It is quite probable that cells which advance from the facial nerve along the chorda tympani enter the primordium of the submaxillary ganglion after the junction of the chorda tympani with the lingual nerve has been effected. The primordium of this ganglion increases in size relatively rapidly. In an embryo 13 mm. in length (no. 485), as illustrated in figure 31, the submaxillary ganglion is represented by a relatively large mass of cells. In sections of embryos 12 mm. and over in length which cut the lingual nerve transversely at the level of the submaxillary ganglion, this mass of cells completely encircles the lingual nerve trunk. This condition obtains for a considerable interval following the 12-mm. stage. In view of the early phase of development represented by embryos 12 and 13 mm. in length, it is inconceivable that any considerable portion of the cell-mass which constitutes the primordium of the submaxillary ganglion at this stage arose from cells which have advanced thither from the facial nerve. Therefore, we must conclude that the submaxillary ganglion arises primarily from cells of trigeminal origin which advance distally along the lingual division of the trigeminal nerve. This conclusion is in accord with the work of Broman ('11) and Streeter ('12). Ganfini ('17) does not admit that in embryos of the guinea-pig and

the pig any cells enter the submaxillary ganglion from sources other than the semilunar ganglion.

In keeping with his conclusion that the sphenopalatine and otic ganglia are derived exclusively from cells which advance peripherally along the greater superficial petrosal and the lesser superficial petrosal nerves, respectively, Stewart ('20) has concluded that the submaxillary ganglion arises exclusively from cells which advance peripherally along the chorda tympani. In view of the intimate relationship of the primordium of the submaxillary ganglion with the lingual nerve, he admits that direct observations can lend little support to this conclusion. Obviously, however, it is demanded by the theory that these several ganglia rise exclusively from cells which advance peripherally along the nerve trunks which later carry the preganglionic fibers to each ganglion respectively.

Sublingual and lingual ganglia

As the lingual nerve grows distally beyond the primordium of the submaxillary ganglion, as observed in embryos 12 mm. and over in length, its fibers are accompanied by numerous migrant cells. Some of these cells have become aggregated in the path of the nerve to give rise to the sublingual ganglion, while others advance along the branches of the lingual nerve to give rise to the smaller ganglionic masses in the tongue which remain associated with the lingual rami. Obviously, the larger sublingual ganglion and the smaller ganglionic masses associated with the rami of the lingual nerve arise from cells whose sources are essentially the same as those of the cells which give rise to the submaxillary ganglion.

The small sympathetic ganglia in the posterior portion of the tongue arise in association with the lingual ramus of the glossopharyngeal nerve. During the early developmental stages this nerve also contains cells of cerebrospinal origin. As the lingual ramus grows into the tongue aggregates of cells occur near its growing extremity (fig. 11, *SLG*). Some of these cell-groups remain closely associated with the nerve trunk, while other cells

advance along its branches and give rise to minute sympathetic ganglia throughout the portion of the tongue which is innervated by the glossopharyngeal nerve.

SOURCES OF THE SYMPATHETIC NEURONES

A review of the literature indicates that all the earlier investigators who recognized the ectodermal origin of the sympathetic nervous system supported the theory that the cells which give rise to the sympathetic primordia are in some manner derived from the cerebrospinal ganglia (or neural crest). Following the introduction of the principle of the migration of these cells by His, Jr. ('91), all, except the advocates of the theory of local differentiation and the multicellular nature of nerve fibers, supported a theory according to which these cells either migrate along the fibrous paths of cerebrospinal nerves and communicating rami or in advance of these fibers either along the paths later occupied by them or directly through the mesenchyme. It was early observed that cells identical in appearance with those which migrate from the spinal ganglia into the primordia of the sympathetic trunks are present in the ventral roots of the spinal nerves from the very beginning of the period of migration. It was also observed that cells of nervous origin migrate from the walls of the neural tube into the motor roots of the spinal and certain of the cranial nerves. Such observations made on embryos of the lower vertebrates, especially the Elasmobranchii, indicate that cells of medullary origin migrate into the motor roots of the spinal nerves in considerable abundance. In embryos of the higher vertebrates an abundant migration of such cells into the motor nerve roots is less apparent. Nevertheless, the recorded observations justify the conclusion that many of the cells which advance peripherally along the spinal nerves are derived from the ventral half of the neural tube. In spite of the knowledge of the presence of these cells of medullary origin in the paths along which cells advance into the primordia of the sympathetic trunks, they have not generally been considered of any consequence in the development of the sympathetic nervous system.

Hoffmann ('00), who made careful observations on Elasmobranch embryos, was among the earliest investigators who concluded that some of the sympathetic elements are derived from the neural tube via the ventral roots of the spinal nerves. Harrison ('01) was led to the same conclusion by his observations on embryos of the salmon. This conclusion was further supported by Harrison's ('04) experimental observations on amphibian larvae. Neumayer ('06), though not an advocate of the migration theory, inferred from his observations on embryos of *Lacerta* and the chick that the sympathetic primordia are derived both from cells in the dorsal and the ventral nerve roots. Carpenter ('06) recognized the cells which migrate from the wall of the mid-brain along the oculomotor and the abducent nerves, in embryos of the chick, as the 'indifferent' cells of Schaper, i.e., cells which have the capacity either to develop into neurones or supporting elements. He further observed that some of the cells of this type associated with the oculomotor nerve become incorporated in the ciliary ganglion.

Froriep ('07) was perhaps the first investigator who vigorously supported the theory that cells of medullary origin which advance peripherally along the motor roots of the cerebrospinal nerves play an important part in the development of the sympathetic nervous system. Indeed, he concluded that all sympathetic neurones are derived from cells which have their origin in the ventral half of the neural tube. His observations were based on embryos of *Torpedo* and the rabbit. Cajal ('08) drew essentially the same conclusion from his observations on embryos of the chick. By the aid of his own specialized technique he recognized elements in the motor roots of the spinal and certain of the cranial nerves as nerve cells in the bipolar phase. His observations show clearly that at least some of the cells which migrate from the medullary tube into the motor nerve roots become differentiated into neurones.

As far as the writer has been able to ascertain, Froriep and Cajal are the only investigators who have supported the theory that the sympathetic neurones are derived exclusively from cells which have their origin in the ventral half of the neural tube and

migrate peripherally along the motor nerve roots. The several other investigators cited above seem to favor the theory that the sympathetic system is derived in part from cells which have their origin in the cerebrospinal ganglia (or neural crest) and in part from cells which have their origin in the ventral half of the neural tube. This theory is supported also by the writer's observations on embryos of types of the several classes of vertebrates as well as by the work of Abel ('12) on embryos of the chick and the extensive work of Ganfini ('11-'18) on embryos of various types of vertebrates.

Held ('09) and Marcus ('09) are among the most recent investigators who still maintain that the sympathetic nervous system is derived exclusively from the cerebrospinal ganglia or the neural crest. From observations made on embryos of Elasmobranchii, Held argued that the cells present in the motor roots of the spinal nerves play no part in the development of the sympathetic trunks because, in these embryos, the primordia of the sympathetic ganglia lie in contact with the sensory and not with the motor nerve roots and there are no cellular connections apparent between the latter and the former. Furthermore, the motor roots apparently contain fewer cells than the sensory roots.

The writer's observations on embryos of *Acanthias* suggest that Held's conclusions are based on observations made on embryos which were somewhat too far advanced in their development to reveal the true relationship of the primordia of the sympathetic trunks to the motor roots of the spinal nerves. As has frequently been observed, cells migrate from the ventral part of the neural tube into the ventral roots of the spinal nerves in great abundance in early elasmobranch embryos. Indeed Balfour ('77) described the ventral nerve root in such embryos as "an elongate cellular structure with a wide attachment to the spinal cord." In transverse sections of early embryos of *Acanthias* stained by the iron-hematoxylin method it may be observed, as the writer has shown in an earlier paper ('11), that some of these cells, as they advance peripherally, become scattered in the mesenchymal tissue along the dorsolateral aspects of the aorta with other cells of neural crest origin and later become

incorporated in the primordia of the sympathetic trunks. In embryos which are somewhat further advanced in their development the primordia of the sympathetic ganglia appear in contact with the sensory and not with the motor roots of the spinal nerves, as described by Held. After this condition obtains the genetic relationship of the sympathetic ganglia to the motor roots of the spinal nerves is no longer apparent.

Neal ('14) has taken exception to these findings. He admits the possibility that cells of medullary origin may enter the sympathetic primordia, but he insists that the present writer has "presented no facts which make this inference seem more certain." Indeed, he does not admit that the evidence presented indicates that cells of cerebrospinal origin become scattered in the mesenchymal tissue along the dorsolateral aspects of the aorta. He seems to regard the differentiation upon which the writer based his conclusion that certain cells present in this mesenchymal tissue in sections of early embryos of *Acanthias* are cells of cerebrospinal origin which have migrated thither as the creation of a too vivid imagination. The interpretation of these cells was based on the size, character, and staining qualities of their nuclei. These are the criteria which have commonly been employed in the recognition of cells of nervous origin lying outside the cerebrospinal nervous system in early embryos. Cells of this type are present in considerable abundance in the mesenchymal tissue along the dorsolateral aspects of the aorta just before the primordia of the ganglia of the sympathetic trunks appear as compact cell-masses, but gradually become less abundant as these cell-masses increase in size. This fact was interpreted as evidence that these cells become incorporated in the primordia of the sympathetic trunks. It might have been pointed out further that it would be quite impossible to account for all the cells present in the motor roots of the spinal nerves in early embryos of *Acanthias* by the number of cells associated with the fibers of these motor roots soon after the primordia of the ganglia of the sympathetic trunks appear as compact cell-masses in contact with the sensory roots of the spinal nerves. Neither can the rapid increase in size of these ganglionic masses following their earliest

appearance be accounted for by migration of cells along the sensory nerve root and local cell division alone.

A study of Neal's paper seems to justify the inference that he does not admit that cells of cerebrospinal origin either migrate in advance of the growing nerve fibers or deviate from the course of the latter. His observations are based largely on material prepared by the method of vom Rath. Since the observations referred to above were published the writer has had occasion to study a series of embryos of *Acanthias* prepared by the vom Rath method. This method brings out the early nerve fibers much more distinctly than does the iron-hematoxylin method; however, it does not differentiate cells of nervous origin from cells of mesenchymal origin as clearly as does the latter method. Doubtless, fibers are present in the nerve roots somewhat earlier than the writer observed them in his earlier work. However, the important question at issue is, do any cells of medullary and neural crest origin deviate from the course of the motor and sensory roots of the spinal nerves respectively as they advance peripherally? For evidence on this point we need not depend on the observations of the present writer nor on embryos of the *Elasmobranchii* alone. As indicated by the work of well-known investigators referred to in this paper, the migration of cells of cerebrospinal origin in advance of the growing nerve fibers and directly through mesenchymal tissue outside the paths of the growing nerves has been observed repeatedly in embryos of various types of vertebrates.

At this point the writer would call attention to the very careful work of Ganfini ('11) on the development of the sympathetic nervous system in fishes. In early embryos of *Amia*, a ganoid type, Ganfini observed that cells of medullary origin which advance peripherally in the motor roots of the spinal nerves deviate from the path of the motor fibers and advancing toward the aorta become scattered in the mesenchymal tissue along its dorsolateral aspects. These cells, according to Ganfini, with cells which advance from the spinal ganglia along the sensory roots of the spinal nerves, become incorporated in the primordia of the sympathetic trunks. These findings in embryos of *Amia* corroborate

the findings of the present writer in embryos of *Acanthias*. Indeed, the evidence seemed so clear to Ganfini that he expressed surprise that, after having described this condition in embryos of *Acanthias*, the writer should have failed to describe it in embryos of *Amia*. By way of explanation it may be said here that the cells of nervous origin did not react to the iron-hematoxylin method in the embryos of *Amia* at the writer's disposal as they did in the embryos of *Acanthias*. Therefore, he was unable to recognize cells of this type scattered in the mesenchymal tissue. It seems entirely probable that the primordia of the sympathetic trunks arise in essentially the same manner both in embryos of *Acanthias* and *Amia*. Therefore, the findings of Ganfini in embryos of *Amia* are highly gratifying.

In view of the more recent work on the development of the sympathetic nervous system, especially the extensive work of Ganfini, the evidence that cells of medullary origin which advance peripherally along the motor nerve roots become incorporated in the sympathetic primordia in embryos of all classes of vertebrates seems to the writer conclusive. That cells of neural-crest origin take part in the development of the sympathetic nervous system has been very generally conceded. The present series of observations on human embryos is in full accord with this conception. Precisely what part the cells from each of these two sources play in the development of the sympathetic nervous system cannot be determined at present.

That both cells of medullary and of neural crest origin enter the primordia of the vagal sympathetic plexuses and certain of the cranial sympathetic ganglia is not apparent. The cells which may be traced from the wall of the hindbrain into the rootlets of the vagi are identical in appearance with the cells which become separated from the distal ends of the ganglia on the vagus trunks and advance farther peripherally; therefore, it is quite impossible to identify cells of medullary origin along the vagi distal to the ganglia on their trunks. Likewise, the cells which migrate from the wall of the hindbrain into the rootlets of the glossopharyngeal nerve cannot be traced with certainty beyond the petrosal ganglion along the lesser superficial petrosal nerve.

Neither can cells of medullary origin in the rootlets of the facial nerve be traced beyond the geniculate ganglion along the greater superficial petrosal nerve. On the other hand, the presence of one or more ganglia on a nerve trunk does not preclude the possibility that cells of medullary origin may advance along the path of the latter. Consequently, cells derived from the walls of the hindbrain may advance along the vagi into the primordia of the vagal sympathetic plexuses or along the lesser superficial petrosal and greater superficial petrosal nerves, respectively, into the otic and sphenopalatine ganglia. Indeed, if we must admit a double origin for parts of the sympathetic nervous system, there is no good reason to assume that any part of it is derived exclusively from cells which have their origin in the neural crest.

This theory of the double origin of the sympathetic nervous system does not imply that all the cells which become differentiated into sympathetic neurones actually migrate from the cerebrospinal nervous system into the sympathetic primordia. As pointed out above, Carpenter ('06) interpreted the cells which migrate from the midbrain along the oculomotor nerve in embryos of the chick as the 'indifferent' cells of Schaper, i.e., cells which have the capacity either to develop into neurones or supporting elements. The writer, in an earlier paper ('10), presented evidence which supports the conclusion that the cells which migrate from the cerebrospinal nervous system toward the sympathetic primordia in mammalian (pig) embryos are of the same type. The present series of observations on human embryos justifies the same conclusion. Schaper ('97) pointed out that the 'indifferent' cells which arise by the mitotic division of the 'germinal' cells of His do not become differentiated at once, but retain the capacity for further division by which they give rise to new generations of indifferent cells which in turn become differentiated into neurones or supporting elements. As observed in the earlier work referred to above, many of the cells of cerebrospinal origin which migrate peripherally undergo mitotic division along the course of migration or in the sympathetic primordia. The cells which migrate toward the sympathetic primordia in human embryos behave in the same manner. Mitotic figures are not un-

common both along the paths of migration and in the primordia of the sympathetic ganglia. Therefore, we must conclude that many of the elements which become differentiated into sympathetic neurones arise by the mitotic division of migrant cells either before or after they have become incorporated in the primordia of the sympathetic nervous system. According to this interpretation, the sympathetic system is entirely homologous with the other functional divisions of the nervous system.

SUMMARY

The primordia of the sympathetic trunks and the prevertebral plexuses arise from cells of cerebrospinal origin which advance peripherally both along the dorsal and ventral roots of the spinal nerves.

The vagal sympathetic plexuses, viz., the pulmonary, the cardiac, and the enteric plexuses, except in the aboral portions of the digestive tube, arise from cells of cerebrospinal origin which advance peripherally along the vagi. In the more distal portions of the digestive tube the enteric plexuses arise from cells which are derived from the sympathetic supply in the lower trunk region.

The majority of the cells which constitute the primordium of the ciliary ganglion are derived from the semilunar ganglion via the ophthalmic nerve. Relatively few cells are contributed via the oculomotor nerve.

The cells which enter the primordium of the sphenopalatine ganglion earliest advance peripherally along the greater superficial petrosal nerve. The majority of the cells which enter the primordium of this ganglion are derived from the semilunar ganglion via the maxillary nerve and its rami.

The primordium of the otic ganglion arises at the growing extremity of the lesser superficial petrosal nerve as an aggregate of cells which advance primarily from the petrosal ganglion. The otic ganglion also receives cells of trigeminal origin via the mandibular nerve and its rami.

The submaxillary and sublingual ganglia arise on the lingual nerve primarily from cells of trigeminal origin. They probably receive some cells of facial origin via the chorda tympani.

The smaller sympathetic ganglia associated with the rami of the glossopharyngeal nerve in the posterior portion of the tongue arise from cells which advance into the tongue along the glossopharyngeal fibers.

The cells which give rise to sympathetic neurones are derived both from the cerebrospinal ganglia and the neural tube. Not all of these cells actually migrate as such from the cerebrospinal nervous system. Many of them arise by the mitotic division of migrant cells along the paths of migration and in the primordia of the sympathetic nervous system.

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PLATES

PLATE 1

EXPLANATION OF FIGURES

13 Human embryo, 7 mm. in length, 617—13—1—3×315. Transverse section through lower thoracic region showing spinal nerve and sympathetic trunk. *a*, aorta; *c*, communicating ramus; *sp*, spinal nerve; *Sy*, sympathetic trunk.

14 Human embryo, 9 mm. in length, 721—13—1—3×335. Transverse section showing ventral root of spinal nerve with migrant medullary cells (*cvr*).

15 Human embryo, 14 mm. in length, 511—9—1—2×160. Sagittal section showing vagus branch to bulbar region of heart with aggregates of cells which become incorporated in cardiac plexus (*cp*).

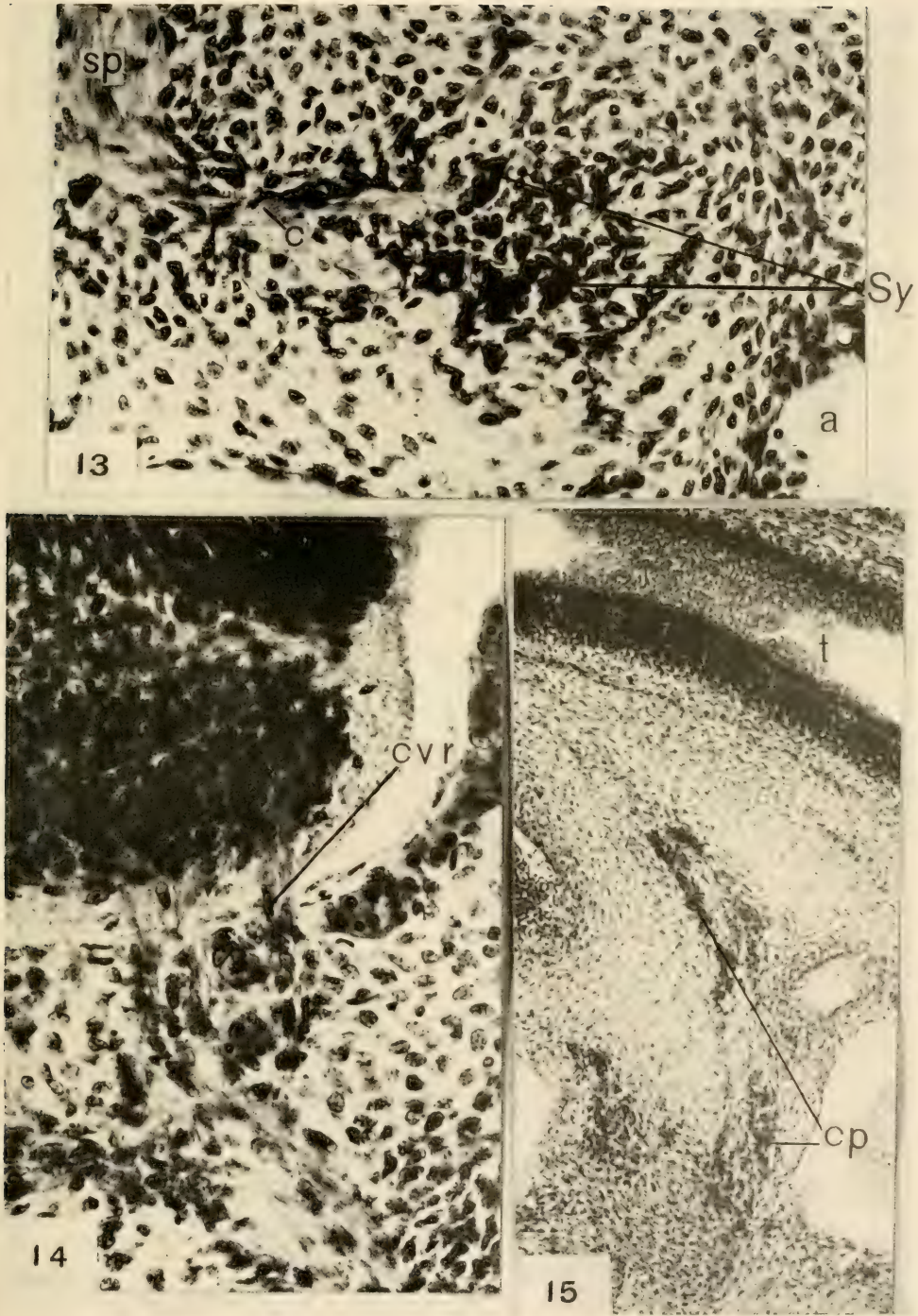


PLATE 2

EXPLANATION OF FIGURES

16 Human embryo, 10.1 mm. in length, 623—16—3—7×160. Transverse section through abdominal region showing primordia of sympathetic trunks and prevertebral plexuses. *a*, aorta; *pv*, prevertebral plexuses; *Sy*, sympathetic trunk.

17 Human embryo, 10.1 mm. in length, 623—15—2—2×160. Transverse section through upper abdominal region showing primordia of sympathetic trunks and prevertebral plexuses. *a*, aorta; *pv*, prevertebral plexuses; *Sy*, sympathetic trunk.

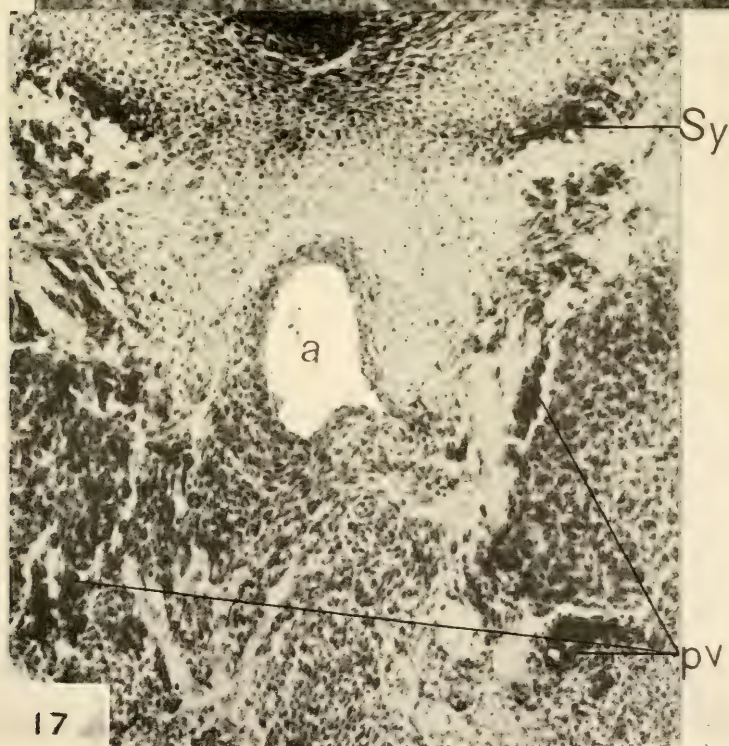
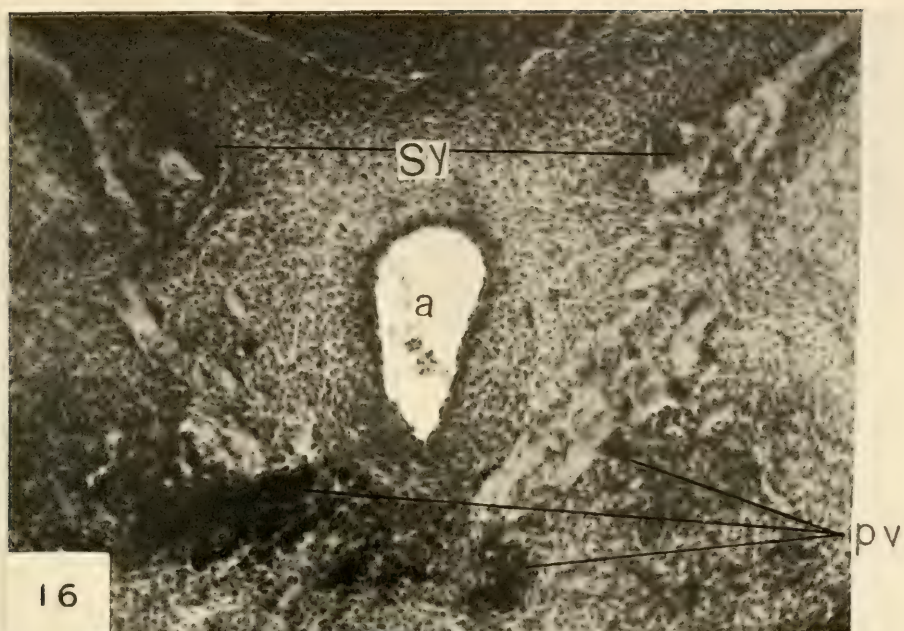


PLATE 3

EXPLANATION OF FIGURES

18 Human embryo, 10.1 mm. in length, 623—10—2—4×240. Transverse section through oesophagus showing vagus trunks and oesophageal plexus. *oep*, cell aggregates in oesophageal plexus; *v*, vagus trunks.

19 Human embryo, 10.1 mm. in length, 623—13—2—2—2×240. Transverse section through oesophagus just above upper level of heart showing oesophageal plexus. *oep*, cell aggregates in oesophageal plexus; *vb*, vagus branches.

20 Human embryo, 10.1 mm. in length, 623—11—2—4×240. Transverse section through roots of lungs showing primordia of pulmonary plexuses. *pp*, cell aggregates in pulmonary plexuses; *vb*, vagus branches.

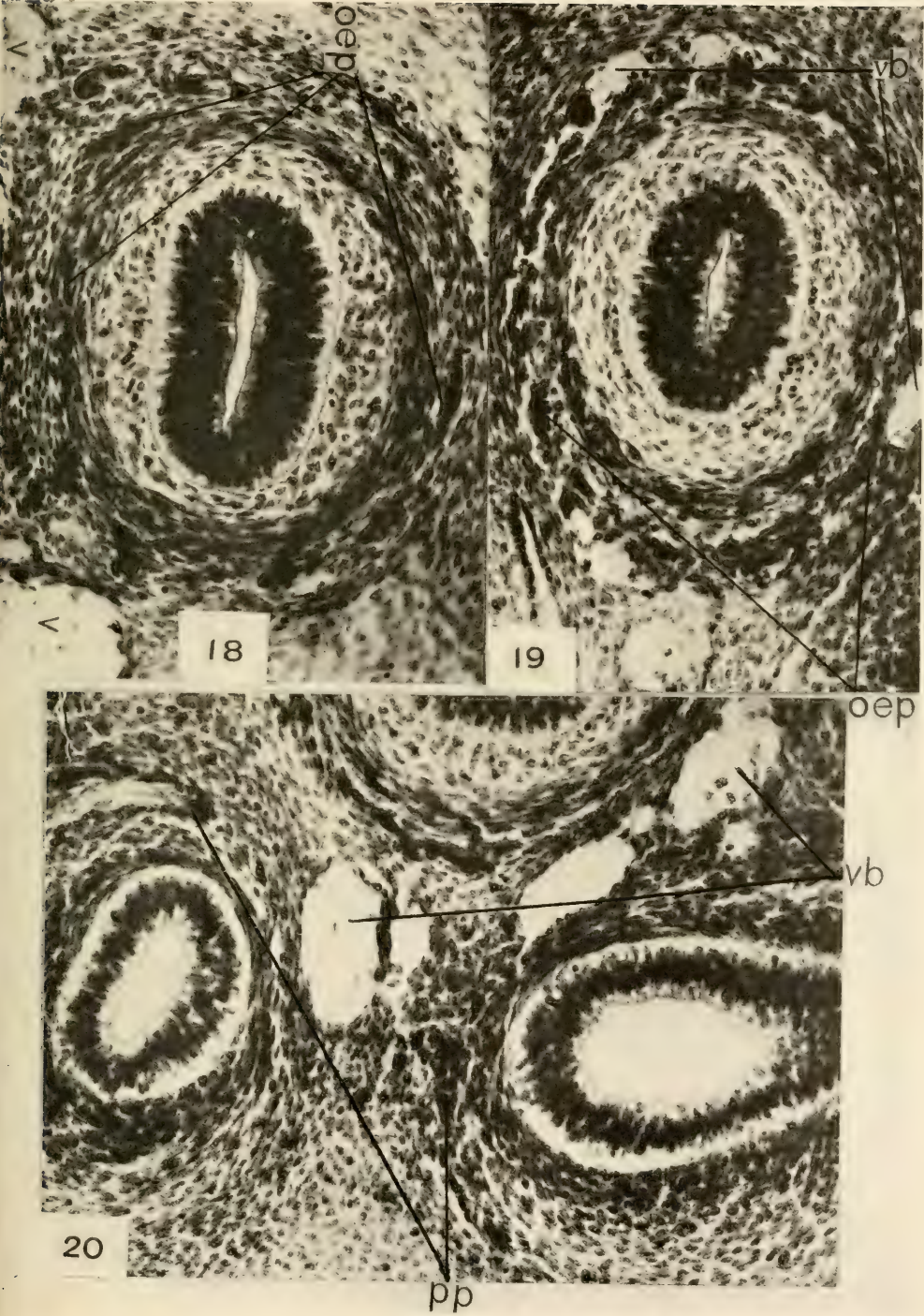


PLATE 4

EXPLANATION OF FIGURES

21 Human embryo, 14 mm. in length, 511—12—2—2×160. Sagittal section through primordium of ciliary ganglion (*cg*). *OCN*, oculomotor nerve; *Op*, ophthalmic nerve.

22 Human embryo, 13 mm. in length, 485—8—2—2×335. Section showing apparent cellular continuity between semilunar and otic ganglia. *Man*, mandibular nerve; *og*, otic ganglion; *SG*, semilunar ganglion.

23 Human embryo, 14.6 mm. in length, 1919—11—2—2×160. Coronal section showing maxillary ramus (*mr*) leading into primordium of sphenopalatine ganglion (*spg*). *gsp*, nerve of the pterygoid canal which includes the fibers of the greater superficial petrosal nerve; *M*, maxillary nerve; *SG*, semilunar ganglion.



PLATE 5

EXPLANATION OF FIGURES

24 Human embryo, 20 mm. in length, 462—15—1—1×335. Section cutting maxillary nerve (*M*) transversely at level of sphenopalatine ganglion (*spg*), showing maxillary ramus (*mr*) into the latter.

25 Human embryo, 20 mm. in length, 462—15—1—1×160. Section showing maxillary ramus (*mr*) and nerve of the pterygoid canal entering sphenopalatine ganglion (*spg*). *GSP*, nerve of the pterygoid canal which includes the fibers of the greater superficial petrosal nerve.

26 Human embryo, 21 mm. in length, 460—16—2—2×130. Section showing maxillary ramus (*mr*) and nerve of the pterygoid canal (*GSP*) entering sphenopalatine ganglion.

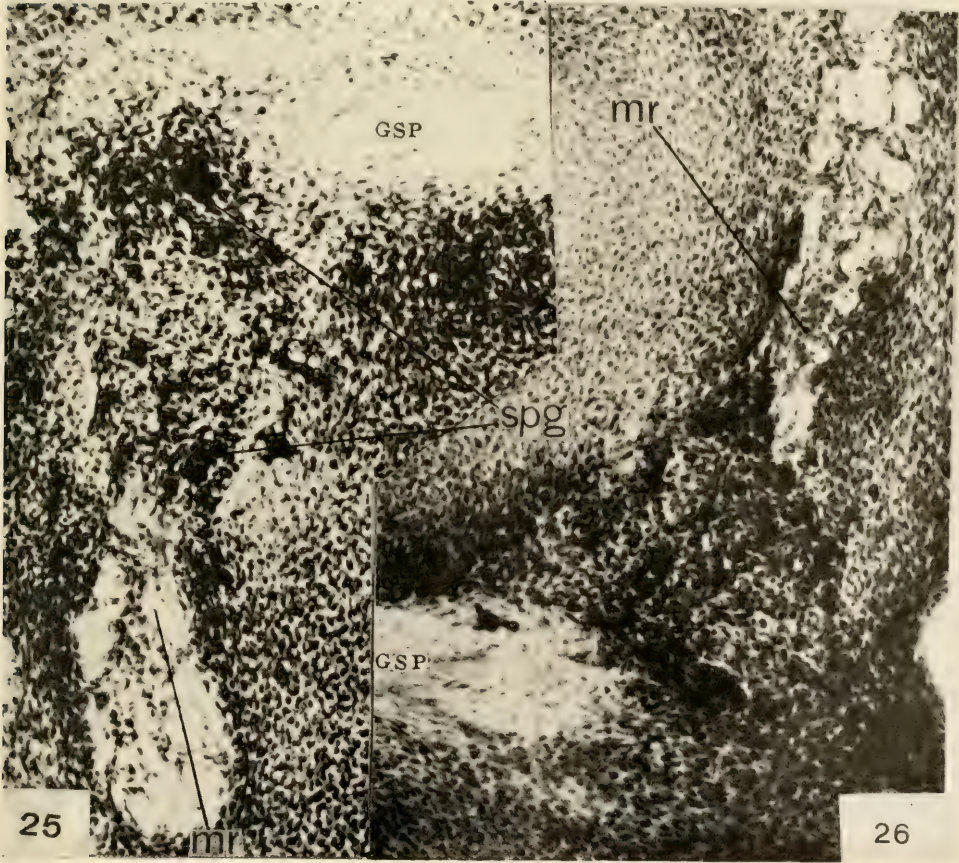
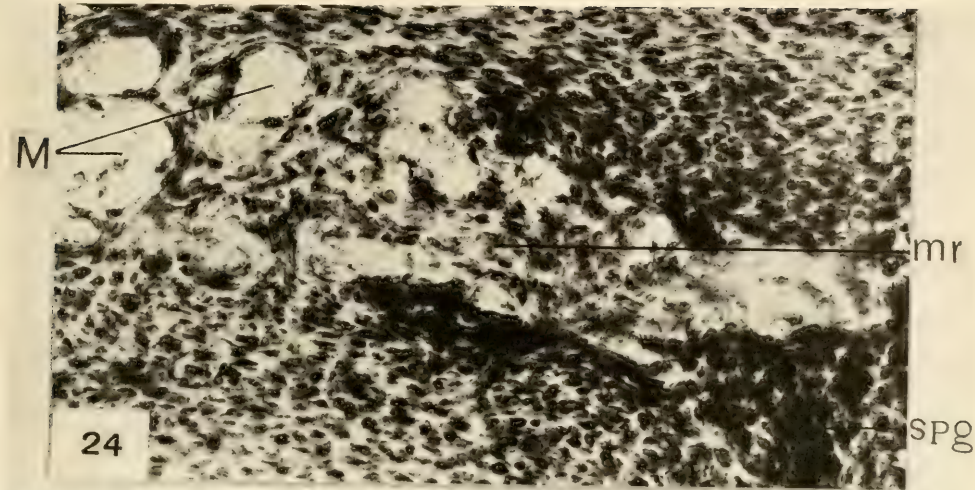


PLATE 6

EXPLANATION OF FIGURES

27 Human embryo, 20 mm. in length, 462—14—2—3×335. Section through mandibular nerve (*Man*) and ramus (*Mnr*) to otic ganglion (*OG*).

28 Human embryo, 21 mm. in length, 460—16—1—2×160. Section cutting mandibular nerve (*Man*) transversely at level of otic ganglion (*OG*).

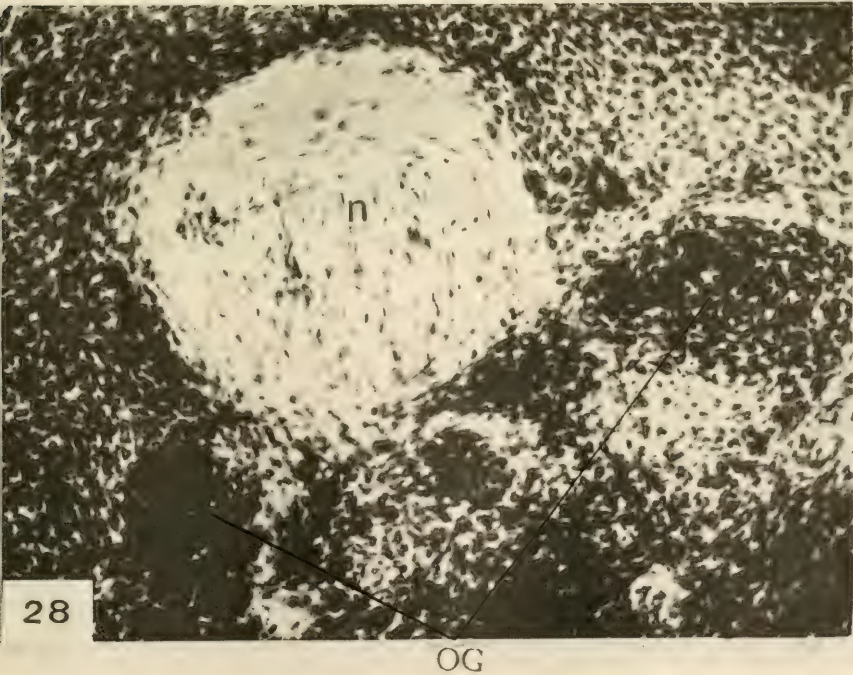
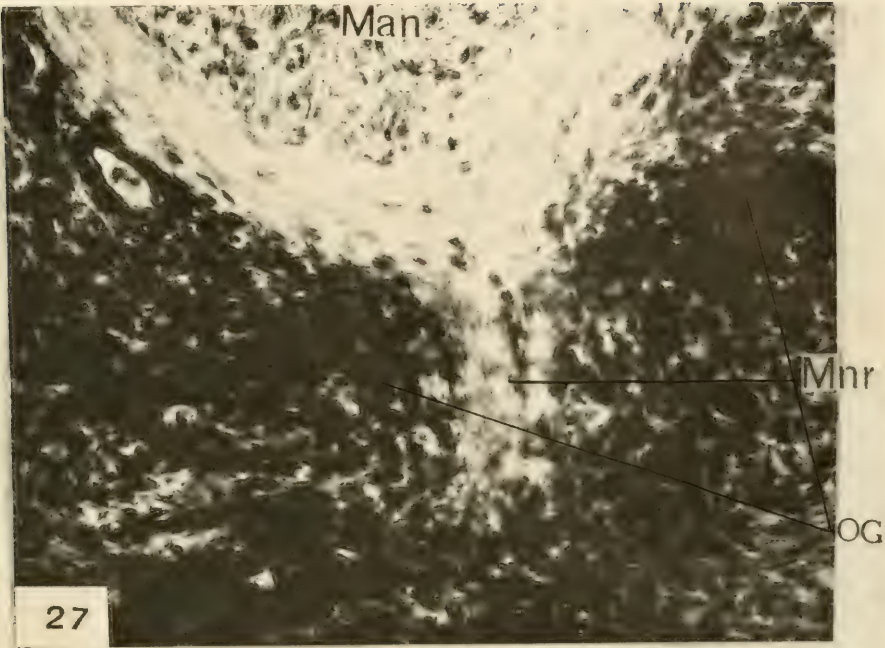


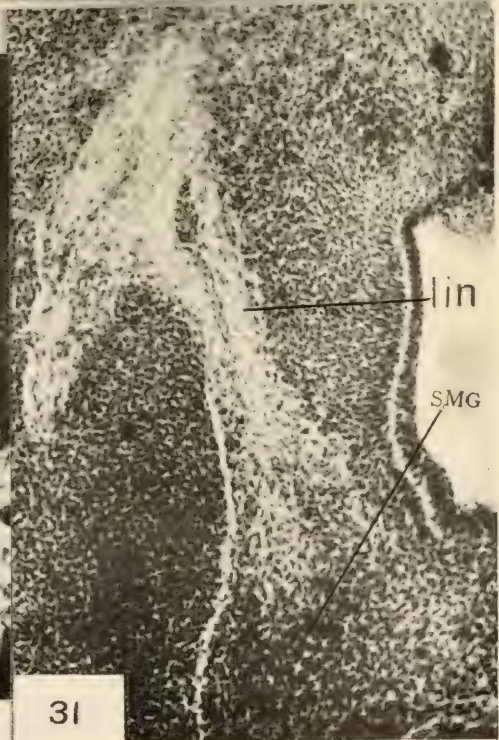
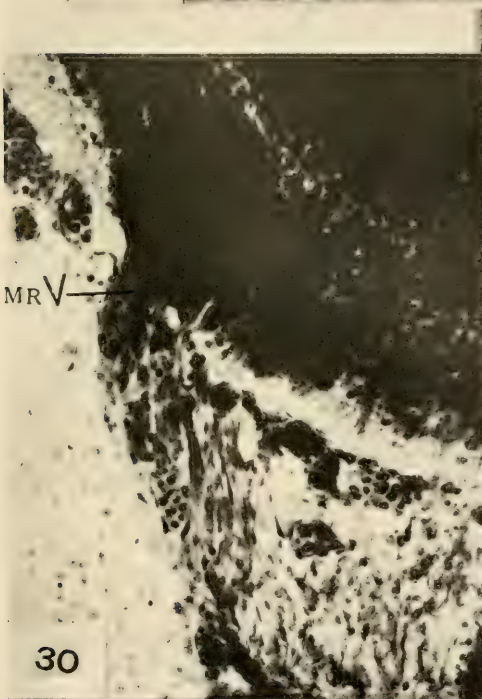
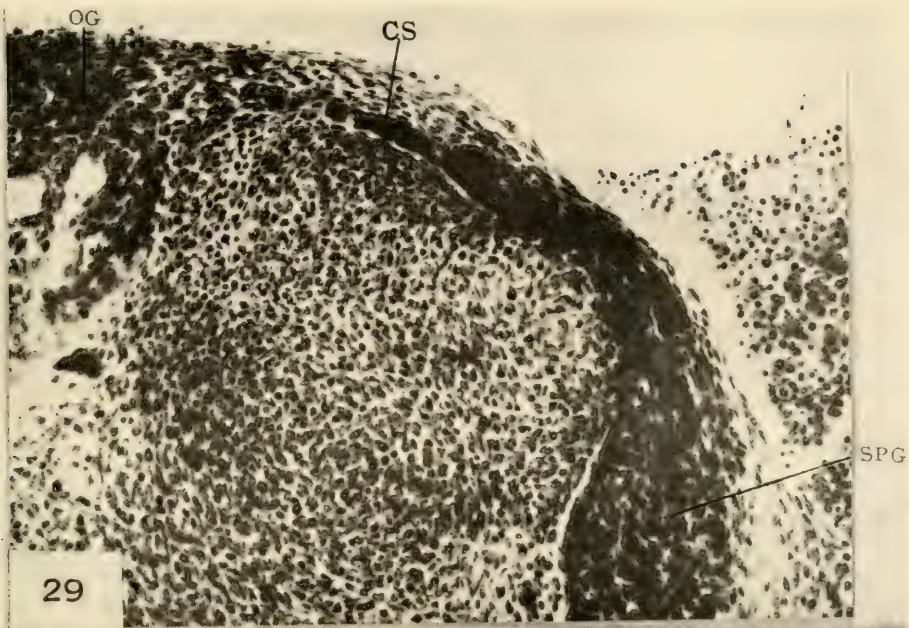
PLATE 7

EXPLANATION OF FIGURES

29 Human embryo, 14 mm. in length, 144—5—2—2×240. Sagittal section showing cellular ramus (*CS*) connecting otic (*OG*) and sphenopalatine (*SPG*) ganglia.

30 Human embryo, 14.5 mm. in length, 1267—8—2—3×315. Section through motor root of trigeminal nerve (*MRV*) showing migrant medullary cells.

31 Human embryo, 13 mm. in length, 485—13—8—3×120. Section showing primordium of submaxillary ganglion (*SMG*). *lin*, lingual nerve.



Resumen por el autor, Kenji Nittono.

Sobre el crecimiento de las neuronas que componen el ganglio de Gasser de la rata albina, desde el nacimiento hasta la madurez.

Las células mas grandes del ganglio de Gasser de la rata albina presentan tres fases en su crecimiento: 1. El crecimiento rápido desde el nacimiento hasta los 20 días; 2. El crecimiento mas lento desde los 20 días hasta los 80 a 100 días, y 3. Una fase final en la cual el crecimiento o es muy lento, o puede tener lugar una ligera atrofia. El núcleo crece del mismo modo que la célula, pero los cambios de tamaño son pequeños. En una edad determinada, el efecto del tamaño del cuerpo sobre el diámetro de las células es positivo, pero de poca importancia. No existe diferencia apreciable de tamaño entre las células del ganglio derecho y las del izquierdo. La madurez morfológica del citoplasma se obtiene a los 20 días, próximamente, pero la relación nucleoplasmática, que es elevada, aumenta mas del doble entre el nacimiento y la pubertad. Antes de los ochenta días el volumen de las células ganglionares aumenta con el área de la cabeza. Los diámetros de las fibras nerviosas en la raíz del quinto nervio son mayores que en las demás ramas. Las fibras crecen después que las células han cesado de crecer. En la madurez, el área del cilindro-eje es en todos los casos la mitad del área de toda la fibra. Después de los ochenta días, el área del eje en las fibras del quinto nervio aumenta con el área de la cabeza. Las neuronas del ganglio de Gasser difieren en varias relaciones de tamaño, y en el periodo de crecimiento difieren de las situadas en el ganglio del séptimo nervio cervical. Alcanzan la madurez mas tarde.

Translation by José F. Nonidez
Cornell Medical College, New York

ON THE GROWTH OF THE NEURONS COMPOSING THE GASSERIAN GANGLION OF THE ALBINO RAT, BETWEEN BIRTH AND MATURITY

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FIVE CHARTS AND ONE PLATE (TWELVE FIGURES)

In the neurological laboratory of The Wistar Institute a systematic study of the growth of the neurons forming the cranial and spinal ganglia of the albino rat is in progress. In a paper by Donaldson and Nagasaka ('18) a series of observations on the later growth of the cells and fibers forming the seventh cervical spinal ganglion have already been reported. The cranial ganglia are of course somewhat specialized and modified, and at the suggestion of Doctor Donaldson I took up the study of the growth of the neurons in the gasserian ganglion to obtain data which might be compared with those already at hand for a typical spinal ganglion.

I was asked to determine the increase in the diameter of the largest cells and their associated fibers in the gasserian ganglion of the albino rat from birth to maturity and to add such other observations as became necessary in the course of the investigation.

MATERIAL AND TECHNIQUE

For this entire study seventy-six normal male albino rats were employed. For the study of the ganglion cells thirty-eight rats were used. These ranged from birth to 485 days in age and from 5.4 to 339 grams in body weight. The data appear in table 1.

For the study of the nerve fibers thirty-nine rats were employed, which ranged from 4 to 485 days in age and from 6.7 to 320 grams in body weight. These data appear in table 2.

TABLE 1

Showing the body weight and body length of thirty-eight male albino rats used for the study of the cells of the Gasserian ganglion, arranged according to age

AGE	BODY WEIGHT	BODY LENGTH
<i>days</i>	<i>grams</i>	<i>mm.</i>
1	5.4	51
1	5.6	55
4	5.3	52
4	6.7	57
8	13.1	69
8	11.7	66
12	21.9	85
12	18.2	79
16	21.1	92
16	19.1	82
20	21.4	81
20	21.0	80
25	24.9	95
25	23.0	93
30	35.0	108
30	40.9	118
35	33.1	109
35	33.4	104
40	46.0	120
40	40.1	115
50	76.1	143
50	74.7	138
65	74.7	144
65	96.9	150
80	157.6	183
80	115.5	178
100	150.0	179
100	194.2	201
150	212.7	197
150	202.6	198
198	191.1	190
198	210.2	199
254	339.0	198
254	195.5	191
330	270.7	218
330	245.5	219
385	254.6	221
485	286.0	230

TABLE 2

Showing the body weight and body length of thirty-nine albino rats used for the study of the nerve fibers of the fifth nerve arranged according to age

AGE	BODY WEIGHT	BODY LENGTH
<i>days</i>	<i>grams</i>	<i>mm.</i>
4	8.5	61
4	6.7	55
8	10.6	67
8	12.8	67
12	13.5	76
12	12.7	75
16	19.6	88
16	17.5	79
20	29.3	103
20	17.5	82
25	18.9	90
25	16.2	84
30	25.5	99
30	44.0	120
35	43.4	119
35	49.5	121
40	58.3	140
40	62.0	138
50	45.0	138
50	37.8	119
55	55.3	129
55	50.1	128
66	68.2	142
66	68.0	144
80	101.9	153
80	99.0	148
100	138.0	160
100	112.0	165
150	158.7	173
150	168.7	193
202	205.0	199
202	207.9	187
260	279.5	229
260	230.0	203
300	226.4	221
300	290.0	194
378	320.0	230
378	165.1	178
485	286.0	240

One old rat, 485 days of age, was used for both purposes and therefore the total number of individual rats was seventy-six. To obtain accurate results two rats of like age were employed where possible. The only exception was in the case of the last pair, which were not of like age, one being 385 and one 485 days old.

All the rats were killed with ether and the body weight and body length recorded, as in tables 1 and 2. The thoracic and abdominal organs were carefully examined, and then after the removal of the brain the gasserian ganglion and nerves were exposed on both sides, but the connective tissue which surrounds the nerves was left untouched because I feared that manipulation might injure them.

For the study of the cells, the ganglion with its nerve was fixed in Bouin's fluid for twenty-four hours according to the procedure described by Sugita ('17). Then the materials were washed for twenty-four hours in running water, run through the alcohols, cleared in xylol, rapidly imbedded in paraffin, cut in sections $8\ \mu$ thick in the horizontal plane, stained with a 1 per cent solution of carbol-thionine, and mounted in acid-free balsam.

To improve the staining I left the sections for ten minutes in an aqueous solution of lithium carbonate before they were put in the thionine.

For the study of the nerve fibers the three branches and the fifth (Vth) nerve were removed close to the ganglion and sometimes with the ganglion. In the case of very young rats—four to eight days old—the ganglion and all its nerves were fixed entire. To prevent distortion the nerves were extended to their normal length on a bit of cardboard and then fixed in a 1 per cent solution of osmic acid for five days. They were then washed for twenty-four hours in water and finally were passed through the alcohols, imbedded, cut in cross-section at $6\ \mu$, and the sections mounted as usual.

The measurement of the ganglion cells was made with a Zeiss microscope in which each division of the micrometer eyepiece equaled $4.47\ \mu$. Twenty-five of the largest cells in each ganglion, namely, five cells from each of five sections, which were chosen

from the middle part of the ganglion at intervals of every five sections, were measured.

The measurement of the ganglion cells is somewhat difficult on account of the irregularity of the outline of the cell body. In the case of both the cell body and the nucleus the two maximum diameters at right angles to each other were those measured.

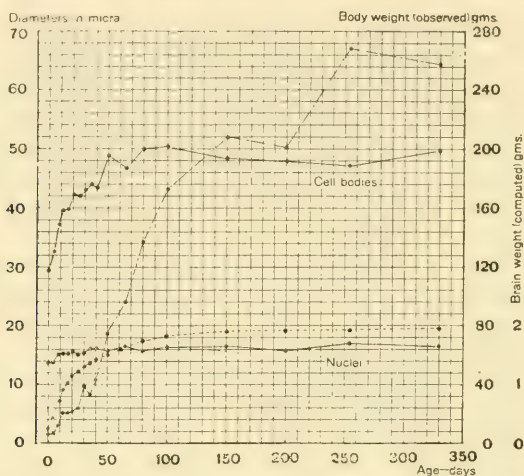


Chart 1 Based on table 3 and giving, on age in days, the diameters of the largest cell bodies in the gasserian ganglion of the albino rat (upper solid graph) and their nuclei (lower solid graph). Ordinate values in μ at the left. Also the observed body weights (upper broken graph), the ordinate values for which are at the right and the computed brain weights (lower broken graph), the ordinate values for which are at the extreme right.

In the case of the cell bodies, the longitudinal diameter was the one which passed through the long axis of the cell, and the transverse diameter was taken at right angles to this on a line passing through the middle of the nucleus. Similarly, in the case of the nucleus, the longitudinal diameter was taken through its longest axis and the width was at right angles to this line and through the middle of the nucleus. The 'computed' diameter which appears in table 3 and those that follow is obtained in each case by taking the square root of the product of the long by the short diameter.

The fibers were cut, as nearly as possible, at right angles to their long axes, which made the cross-section of a myelinated

fiber nearly circular in outline. In this case but a single measurement of the diameter of the entire fiber and of the axis cylinder was made with a Zeiss system in which each division on the ocular scale was equal to 1.3μ . Ten of the largest fibers in a single section were thus measured for each locality.

TABLE 3

Average diameters in μ of the cells and the nuclei according to the age of the rats, based on the full data. At each age the values given are averages from three ganglia

AGE	MEAN BODY WEIGHT	DIAMETERS					
		Cells			Nuclei		
		Long	Short	Computed	Long	Short	Computed
<i>days</i>	<i>grams</i>						
1	5.5	31.2	27.9	29.4	14.9	12.8	13.8
4	5.9	35.3	30.1	32.6	15.0	12.9	13.9
8	12.4	41.0	33.8	37.3	16.3	13.8	15.0
12	20.1	44.1	37.8	39.7	16.7	14.0	15.3
16	20.1	44.7	35.1	39.8	16.7	14.0	15.3
20	21.2	47.1	37.9	42.2	16.9	14.3	15.6
25	24.0	46.2	38.3	42.0	16.6	13.9	15.2
30	38.0	48.4	38.1	42.8	16.8	14.1	15.4
35	33.3	49.5	39.2	44.0	17.7	14.8	16.1
40	43.1	47.5	39.4	43.3	17.8	14.6	16.1
50	75.4	54.0	44.1	48.8	17.3	14.5	15.8
65	85.8	52.9	41.0	46.6	18.3	15.5	16.5
80	136.6	55.5	45.1	50.0	17.7	14.3	15.9
100	172.1	55.8	45.4	50.3	18.0	14.6	16.2
150	207.7	53.8	43.4	48.3	18.1	14.6	16.3
198	200.7	53.5	43.2	47.9	17.0	15.1	15.9
254	267.3	52.6	41.1	47.1	19.2	15.3	17.1
330	258.1	54.7	44.4	49.6	17.8	15.3	16.5
Ratios: 1-330 days				1:1.69			1:1.20

GROWTH IN DIAMETER OF THE CELL BODY AND THE NUCLEUS OF THE LARGEST CELLS IN THE GASSERIAN GANGLION

The original data are based on the measurements taken from the twenty-five largest ganglion cells in the gasserian ganglion of thirty-eight albino rats according to age. For the present discussion these have been condensed as in table 3, and the data arranged according to age.

Each age group contains measurements obtained from seventy-five of the largest ganglion cells contained in three ganglia belonging to two rats of the same age. Table 4 gives the same data arranged according to the mean body weight taken from two rats of the same age. The data from the rats 385 and 485 days old have been omitted from tables 3 and 4 because they represented only single individuals.

Chart 1 shows graphically the data given in table 3 in which the ordinates give average diameters of the cell bodies and the nuclei of the gasserian ganglion on age. I have entered also

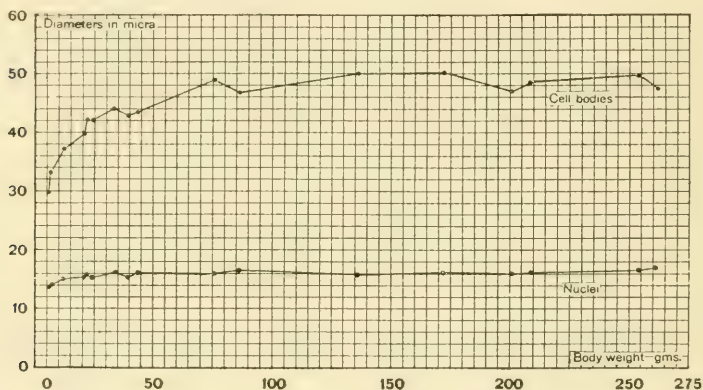


Chart 2 Based on table 4 and giving on body weights the diameters of the largest cells from the gasserian ganglion of the albino rat and of their nuclei.

on this chart the observed body weights and the brain weights (computed) normal to the age.

Chart 2 shows graphically the data given in table 4 in which the diameters of the cell bodies and the nuclei are plotted on the average body weight. The graphs given in these two charts show slight differences in detail, yet the general relations are similar. On these charts three phases may be distinguished in the growth of the cell body and the nucleus. The first phase is represented by a very rapid growth of the cell body to about the first twenty days after birth.

In the second phase the rate of growth diminishes, but still continues to be fairly rapid to about seventy-five to eighty days

or 130 to 160 grams in body weight. The third phase represents the remainder of our records, and during this phase the diameter of the cell body remains nearly constant, or even diminishes slightly, with both body weight and age.

TABLE 4

Average diameters in μ of the cells and the nuclei according to the body weight of the rats, based on the full data. Conditions as in table 3

AGE	MEAN BODY WEIGHT	COMPUTED DIAMETERS	
		Cells	Nuclei
<i>days</i>	<i>grams</i>		
1	5.5	29.4	13.8
4	5.9	32.6	13.9
8	12.4	37.3	15.0
12	20.1	39.7	15.3
16	20.1	39.8	15.3
20	21.2	42.2	15.6
25	24.0	42.0	15.2
35	33.3	44.0	16.1
30	38.0	42.8	15.4
40	43.1	43.3	16.1
50	75.4	48.8	15.8
65	85.9	46.6	16.5
80	136.6	50.0	15.9
100	172.1	50.3	16.2
198	200.7	47.9	15.9
150	207.7	48.3	16.3
330	258.1	49.6	16.5
254	267.3	47.1	17.1
Ratios.....	1:48.6	1:1.60	1:1.24

The end of the first phase corresponds to about twenty days of age or a body weight of about 21.8 grams. This body weight agrees well with the tabular value given by Donaldson ('15).

The end of the second phase corresponds to about seventy-five to eighty days in age or 130 to 160 grams in body weight. The animals used may therefore be considered as normal in size.

During the first two phases the nuclei of the ganglion cells change in size in the same sense as the cell bodies to which they belong, but the amount of change is very small. It is to be

noted, however, that the nuclei do not show the shrinkage indicated by the cell bodies during the last phase.

In chart 1 I have also given a graph for the body weights of the rats here used.

COMPARISON BETWEEN THE LARGER AND SMALLER ANIMALS OF THE SAME AGE

The pairs of rats of like age often differed considerably in body weight. I have attempted therefore to determine to what

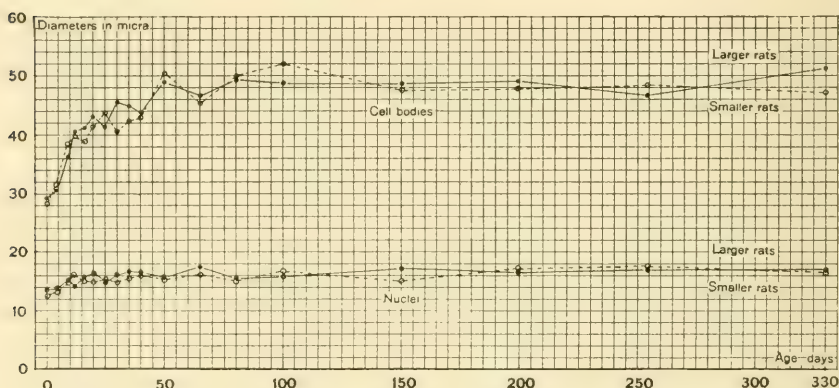


Chart 3 Based on table 5 and giving on age in days the diameters of the largest cells from the gasserian ganglion of the albino rat, and of their nuclei, in rats of like age but of different body weights.

extent the difference in body weight influences the growth of the cell body and the nucleus.

Table 5 (based on the original data) gives the values for the large and the small rats having the same age, and these values are used for chart 3 in which the average diameters of the cell body and the nucleus are plotted on the body weight. From table 5 it is clear that the diameters of the cell bodies and the nuclei of the larger animals are on the average slightly greater than those of the smaller rats.

The number of cases in which the larger animals have the greater cell body amounts to eleven out of eighteen, or 61 per

cent, and the cases in which the larger animals have the greater nucleus, thirteen out of eighteen cases, or 72 per cent. The averaged values given at the bottom of each column in table 5 show that the larger animals possess larger cell bodies and nuclei, though the average differences are very slight indeed.

TABLE 5

Showing the diameters in μ of the cells and the nuclei belonging to the larger and the smaller rats having the same age

AGE	BODY WEIGHT		COMPUTED DIAMETERS			
	Larger rats	Smaller rats	Cells		Nuclei	
			Larger rats	Smaller rats	Larger rats	Smaller rats
<i>days</i>						
1	5.6	5.4	28.9	28.2	13.5	12.5
4	6.4	5.3	30.4	31.4	13.7	13.3
8	13.1	11.7	36.1	38.5	15.2	15.0
12	21.9	18.2	40.5	39.8	14.0	16.2
16	21.1	19.1	41.1	38.6	15.7	15.2
20	21.4	21.0	42.9	41.1	16.2	15.0
25	24.9	23.0	41.1	43.8	15.0	15.2
30	40.9	35.0	45.5	40.5	16.0	14.8
35	33.4	33.1	44.8	42.1	16.5	15.5
40	46.0	40.1	43.8	42.8	16.4	16.0
50	76.1	74.7	48.8	50.2	15.7	15.6
65	96.9	74.7	46.6	45.2	17.3	16.2
80	157.6	115.5	49.5	49.8	15.4	15.2
100	194.2	150.0	48.5	52.1	15.9	16.4
150	212.7	195.5	48.5	47.6	16.9	14.9
198	210.2	191.1	49.2	48.9	16.5	17.0
254	339.0	195.5	46.6	48.5	17.1	17.4
330	270.4	245.5	51.3	47.3	17.0	16.9
Averages....	99.6	81.2	43.6	43.2	15.8	15.4
Ratios.....		1:0.82		1:0.99		1:0.97

The average body weight of the larger animals is 99.6 grams, while that of the smaller ones is 81.2 grams; the ratio between them being 1:0.82. The ratio for the cell bodies is 1:0.99 and the ratio for the nuclei 1:0.97. Thus the difference found in the cell bodies and the nuclei in the two groups is relatively slight and much less than that in the average body weights. If

the observations are limited to the young animals, before eighty days of age, the following results are found:

	MEAN BODY WEIGHT	MEAN DIAME- TER CELL BODY	MEAN DIAMETER NUCLEUS
	<i>grams</i>	μ	μ
Larger animals.....	34.0	40.9	15.4
Smaller animals.....	30.1	40.2	15.0
Ratio.....	1:0.89	1:0.98	1:0.97

In these younger rats the difference of the averaged body weights is smaller than that for the total average. If, therefore, the size of the cell bodies and nuclei follows closely the body weight, their differences should decrease as the difference in the body weights decreases. This does not occur. The relations between the cell bodies and the nuclei remain about the same as those for the entire series. We conclude, therefore, that in albino rats of the same age but of dissimilar body weights, the smaller animal tends to have slightly smaller cells and nuclei in the gasserian ganglion, but that this ganglion, like the central nervous system, is but little influenced by the conditions which cause moderate deviations in the body weight.

COMPARISON BETWEEN THE RIGHT AND LEFT SIDES

The comparison was made in nineteen cases in this series in which the ganglia from both sides were examined. The results are given in table 6.

From table 6 we find that the average values of the diameters of the ganglion cells and the nuclei are slightly greater on the right side than on the left. On the right side the cell bodies and nuclei give 44.2 μ and 15.9 μ , respectively, while on the left they give 44.0 μ and 15.7 μ . However, the difference between right and left is so slight that we are not justified in attaching any significance to it, especially as the plus and minus cases are also nearly equal in number.

THE RATIOS OF THE ENLARGEMENT OF THE CELL BODY AND THE
NUCLEUS AND THE RATIOS OF THE VOLUME OF THE CYTO-
PLASM TO THE VOLUME OF THE NUCLEUS

To examine the relation between the cell size and nuclear size the original data were arranged in six groups, as are given in table 7, which contains all the data, taken from thirty-eight

TABLE 6

Comparison between the cells and the nuclei from the right and left sides of the same rats; on body weight. Diameters in μ

AGE	BODY WEIGHT	CELLS		NUCLEI	
		Right	Left	Right	Left
<i>days</i>	<i>grams</i>	μ	μ	μ	μ
1	5.4	31.4	28.2	15.2	12.5
4	6.4	30.4	36.0	13.7	14.7
8	13.1	36.1	37.4	15.2	14.7
16	21.1	39.0	41.1	15.0	15.7
20	21.4	42.9	42.7	16.2	15.4
12	21.9	40.7	42.2	14.0	15.6
25	24.9	41.0	41.1	15.3	15.0
35	33.4	44.7	45.4	16.5	16.4
30	40.9	45.5	42.7	16.0	15.3
40	46.0	43.2	43.8	15.9	16.4
50	74.7	50.2	47.3	15.6	15.6
65	96.9	48.0	46.6	16.8	17.3
100	150.0	52.1	50.4	16.4	16.2
80	157.6	51.0	49.5	16.7	15.4
254	195.5	48.5	46.2	17.4	16.7
198	210.2	47.2	48.4	16.5	15.7
150	212.7	48.9	48.5	17.0	16.9
385	254.6	47.0	50.4	16.1	16.4
330	270.7	51.3	47.8	17.0	16.1
Averages		44.2	44.0	15.9	15.7
Percentage on left side			(99.8%)		(98.7%)

albino rats from 5.3 grams to 330 grams in body weight and from birth to 485 days in age.

The values for the first group were taken as 1.00. In the case of the cell body, the ratios of the enlargement increase rapidly from the first group to the second, show a relatively slow increase up to the fourth group (87.6 grams in body weight), reach the

maximum at the fifth group (189.2 grams in body weight), and then remain nearly constant. On the other hand, the nuclei show slighter changes in the values of ratios from birth to old age, indicating a less rapid increase in size. These relations are shown by the graphs in charts 1, 2, and 3.

The ratios of the volumes of the cytoplasm to the volumes of the nucleus were calculated according to the following formula:

$$(DC^3 - DN^3) / DN^3 = \text{Ratio}$$

where DC = cell diameter, DN nucleus diameter.

TABLE 7

Showing the increase in the cell body and the nucleus as well as relative size of the cell body and the nucleus for the increasing body weight of the rats—in six groups on body weight

NUMBER OF RATS	BODY WEIGHT	AVERAGE BODY WEIGHT	AVERAGE AGE	CELL BODY		NUCLEI		RATIO OF VOLUME OF CYTOPLASM TO VOLUME OF NUCLEI
				Mean diameter	Ratio of enlargement	Mean diameter	Ratio of enlargement	
	grams	grams	days	μ		μ		
6	5.3-13.1	7.9	4.3	33.2	1.00	14.2	1.00	1:11.8
8	18.2-24.9	21.3	18.3	41.2	1.24	15.3	1.08	1:18.4
6	33.1-46.0	38.1	35.0	43.4	1.31	15.5	1.09	1:21.0
5	74.7-115.5	87.6	62.0	48.0	1.45	16.1	1.13	1:25.5
8	150.0-212.7	189.2	153.8	48.8	1.47	16.3	1.15	1:25.8
5	245.5-339.0	279.1	317.0	48.6	1.46	16.4	1.15	1:25.0

The data thus obtained reveal several interesting relations. The ratio given by the first group (table 7) is 1.0:11.8. This, however, increases very rapidly to 1.0:18.4 for the second group, but the change becomes slower up to the fifth group in which the ratio is 1.0:25.7, and thereafter it remains nearly constant. Thus in the earlier phases of growth the enlargement of the cell body is more rapid than that of the nucleus. This process goes on steadily until the ratio reaches a maximum at the fourth group. The differences which exists between the last three groups are too small to be considered as significant. It is thus evident that during the growth of the cell body and nucleus the ratio more than doubles, and this doubling occurs before puberty, but after that age neither the cytoplasm nor

the nuclei grow appreciably, as can be seen by the columns giving their respective diameters in table 7.

THE RELATION BETWEEN THE RELATIVE VOLUMES OF THE GANGLION CELLS AND THE RELATIVE AREAS OF THE HEAD

It was noted by Levi ('08), by Busacca ('16), and by Donaldson and Nagasaka ('18) that the volume of the spinal ganglion cells increases during later postnatal growth at the same rate as the area of the body surface. I have attempted to determine whether or not the cells of the gasserian ganglion, a cranial ganglion, differ from the spinal ganglion cells in respect of this relation.

In the present case the relative area of the head was used instead of that for the entire body surface, for the simple reason that the fifth nerve innervates the skin and other structures in the head. Just as the relative area of the body surface is found from the squares of the cube roots of the body weight, I have estimated the relative area of the skin of the head from the squares of the cube roots of the weight of the head.¹

The values for the weight of the heads were calculated from the table of Jackson and Lowrey ('12) for the several body weights obtained in the present investigation.

In the first column in table 8 are given the squares of the cube roots of the head weights from which the series of ratios were obtained. Table 8 shows the area of the head as growing much more rapidly than the volume of the ganglion cells.

¹ It is recognized of course that the distribution of the fifth nerve is to the anterior portion of the head only and that the whole head therefore includes a large surface outside of the area supplied by this nerve. Also it is evident that the fore part of the head changes in shape with age. On considering all the relations involved, it would appear that, owing to the increase in the specific gravity of the head tissues with age, the computation here made would give in the older heads, with a higher specific gravity, a computed area which was too large. At the same time the change in the form of the head, which becomes more pear-shaped and less spherical with advancing age, brings about an increase in the actual area of the head in relation to its weight, and we have considered this as balancing the error introduced by the change in the specific gravity of the parts. The direct measurement of the areas of the head at different ages is of course needed for a precise discussion of the question here raised.

This result differs from that reported by Donaldson and Nagasaka ('18), in which the volume of the spinal ganglion cells increased in the proportion of the increase in the area of the entire body. It is important to note, however, that the difference in this relation is accompanied by a difference in the behavior of the ganglion cells themselves in the two localities.

TABLE 8

Showing the relative areas of the head and the relative volumes of the ganglion cells—on body weight

AVERAGE BODY WEIGHT	RELATIVE AREAS OF HEAD				RELATIVE VOLUMES OF GANGLION CELLS μ^3			
	Weight of head		Ratios					
<i>grams</i>	<i>grams</i>							
7.9	$\sqrt[3]{1.9^2}$:	$\sqrt[3]{24.3^2}$:: 1.0 : 5.46	33.2 ³	:	48.6 ³	:: 1.0 : 3.13
21.3	$\sqrt[3]{4.5^2}$:	$\sqrt[3]{24.3^2}$:: 1.0 : 3.08	41.2 ³	:	48.6 ³	:: 1.0 : 1.64
38.1	$\sqrt[3]{6.9^2}$:	$\sqrt[3]{24.3^2}$:: 1.0 : 2.31	43.4 ³	:	48.6 ³	:: 1.0 : 1.40
87.6	$\sqrt[3]{10.1^2}$:	$\sqrt[3]{24.3^2}$:: 1.0 : 1.79	48.0 ³	:	48.6 ³	:: 1.0 : 1.15
189.2	$\sqrt[3]{17.9^2}$:	$\sqrt[3]{24.3^2}$:: 1.0 : 1.23	48.8 ³	:	48.6 ³	:: 1.0 : 0.99
279.1	$\sqrt[3]{24.3^2}$:	$\sqrt[3]{24.3^2}$:: 1.0 : 1.00	48.6 ³	:	48.6 ³	:: 1.0 : 1.00

TABLE 9

Data on the relative areas of the head and the relative volumes of the ganglion cells in rats younger than sixty-two days

AVERAGE BODY WEIGHT	RELATIVE AREAS OF HEAD				RELATIVE VOLUMES OF GANGLION CELLS μ^3			
	Weight of head		Ratios					
<i>grams</i>	<i>grams</i>							
7.9	$\sqrt[3]{1.9^2}$:	$\sqrt[3]{10.1^2}$:: 1.0 : 3.05	33.2 ³	:	48.0 ³	:: 1.0 : 3.04
21.3	$\sqrt[3]{4.5^2}$:	$\sqrt[3]{10.1^2}$:: 1.0 : 1.71	41.2 ³	:	48.0 ³	:: 1.0 : 1.58
38.1	$\sqrt[3]{6.9^2}$:	$\sqrt[3]{10.1^2}$:: 1.0 : 1.29	43.4 ³	:	48.0 ³	:: 1.0 : 1.35
87.6	$\sqrt[3]{10.1^2}$:	$\sqrt[3]{10.1^2}$:: 1.0 : 1.00	48.0 ³	:	48.0 ³	:: 1.0 : 1.00

While in the spinal ganglion the cells continue to increase in volume so long as the body increases in area, the corresponding cells in the gasserian ganglion reach nearly their full volume at puberty, and hence do not follow the postpubertal growth of the entire head. This state of affairs has led me to make a comparison of the area of the head during the time when the largest ganglion cells of the gasserian ganglion were increasing in volume, i.e., prior to puberty. The results are presented in table 9.

We here find (table 9) that the volume of the ganglion cells of the gasserian ganglion increases at the approximately same rate as the area of the surface of the head during the period in which the gasserian cells are growing. There is, therefore, a similarity in the behavior of these specialized cells while they are still growing to those in a typical spinal ganglion.

THE NERVE FIBERS

The nerve fibers from the first (ophthalmic), the second (maxillary), the third (mandibular), branches and the root of the Vth nerve were studied on thirty-nine normal albino rats. The body weights in this series ranged from 6.7 grams to 320 grams and the ages from four days to 485 days. The original data represent the averages of the ten largest fibers arranged according to their ages. From the original table thus drawn up the author has made the condensed table 10. From the condensed table the oldest rat was omitted, thus leaving thirty-eight animals, and the data for these are presented in nineteen groups, each group representing two rats of like age.

Table 10 gives the average values from 4 to 378 days in nineteen age groups. The same data as given in table 10 have been arranged also according to body weight, but the latter shows almost the same relations as table 10, and is therefore not printed.

Chart 4 shows graphically the data given in table 10. The ordinates represent the average diameter of the fibers and the abscissas the ages.

THE DIAMETER OF THE NERVE FIBERS

Among four different sets of nerve fibers, table 10 shows that those fibers belonging to the first (ophthalmic) branch give the smallest average diameters which measure 7.6μ and the axis cylinders 5.4μ . The largest average diameters are given by the fibers belonging to the fifth nerve root, and these measure 11μ and the axis cylinders 7.8μ .

Those fibers belonging to the second and the third branches measure $10.2\ \mu$ and $10.2\ \mu$, respectively, while the corresponding axis cylinders measure $7.0\ \mu$ and $7.1\ \mu$. The fibers in the last two branches show, therefore, about the same diameters.

From chart 4 we can clearly distinguish in the fibers three different phases of growth such as were noted for the growth of the cell bodies. Thus the diameters of all the fibers increase very rapidly from the fourth day after birth up to twenty days in

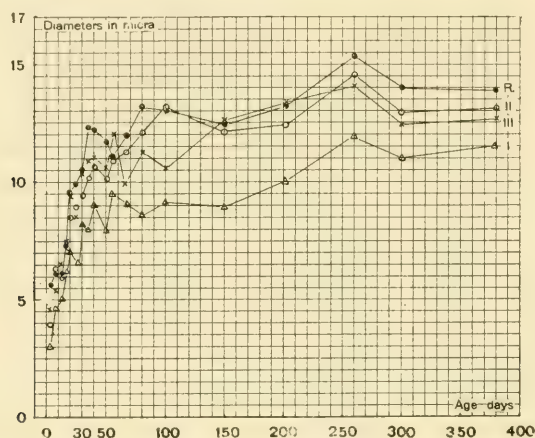


Chart 4 Based on table 10, giving, on age in days, the diameters of the largest entire fibers in the root and branches of the fifth cranial nerve of the albino rat. R = graph for the fibers in the root; I = graph for the fibers in the R. ophthalmicus; II = graph for the fibers in the R. maxillaris; III = graph for the fibers in the R. mandibularis.

age (23.4 grams in body weight), and this rapid increase becomes slower until eighty to one hundred days in age (100.5 to 125 grams in body weight). After this the fibers, however, continue to grow steadily but very slightly throughout the period of the observations.

These results thus approximately correspond to those representing the growth in the diameters of the spinal ganglion cells and fibers (Donaldson and Nagasaka, '18), with one difference: the cell bodies in the gasserian ganglion reach a maximum at an earlier period (about puberty) and then remain nearly constant,

while the fibers after puberty increase very slowly in diameter. In the case of the cells and fibers of the spinal ganglion, however, both grow vigorously after puberty.

TABLE 10

Data on the diameter in μ of the fibers and the axis cylinders taken from three different branches and the fifth nerve root arranged according to age

AGE	MEAN BODY WEIGHT	DIAMETERS							
		First branch		Second branch		Third branch		Fifth nerve root	
		Entire fiber	Axis	Entire fiber	Axis	Entire fiber	Axis	Entire fiber	Axis
<i>days</i>	<i>grams</i>								
4	7.6	3.0	1.8	3.7	2.5	4.6	3.5	5.7	4.2
8	11.7	4.6	3.1	6.3	4.2	5.4	3.2	6.1	3.9
12	13.1	5.0	3.2	5.9	4.0	6.6	4.6	6.1	4.3
16	18.6	6.1	4.1	7.0	4.6	7.5	5.3	7.3	5.1
20	23.4	7.0	4.7	8.5	5.8	9.4	6.1	9.5	6.3
25	17.6	6.6	4.3	8.9	6.3	8.6	5.7	9.8	6.4
30	34.8	8.2	5.4	9.3	6.1	10.5	7.2	10.5	7.2
35	46.5	8.0	5.0	10.2	6.8	10.8	7.6	12.3	8.5
40	60.2	9.0	6.0	10.7	7.3	11.1	8.0	12.2	8.5
50	41.4	7.9	4.7	10.1	6.7	10.6	7.2	11.7	8.4
55	52.7	9.5	6.5	10.9	7.0	12.1	8.5	11.1	7.6
66	68.1	9.1	5.8	11.3	7.4	9.9	6.9	11.9	8.3
80	100.5	8.6	5.9	12.1	8.2	11.3	7.3	13.2	9.5
100	125.0	9.2	6.3	13.2	9.8	10.6	7.5	13.1	9.9
150	163.7	8.9	6.2	12.1	8.1	12.6	9.3	12.4	8.9
202	206.5	10.0	7.0	12.4	9.3	13.3	10.0	13.2	9.0
260	254.8	11.8	8.6	14.6	11.2	14.1	10.0	15.3	11.4
300	258.2	11.0	7.2	12.9	9.4	12.4	8.5	14.0	10.4
378	242.6	11.5	7.5	13.1	9.0	12.7	8.9	13.8	9.6
Averages		7.6	5.4	10.2	7.0	10.2	7.1	11.0	7.8
Ratios		1:3.8	1:4.2	1:3.5	1:3.6	1:2.8	1:2.5	1:2.4	1:2.3

A COMPARISON OF THE GROWTH OF THE NERVE FIBERS IN LARGER AND SMALLER ANIMALS OF THE SAME AGE

I have discussed earlier the relation of the growth of the ganglion cells in the larger and the smaller animals in the same age. The present observation on the fibers was made for the same purpose. Table 11 shows clearly that the mean diameters of

the entire fibers taken from the larger animals are larger than those taken from the smaller animals. More precisely, we find three instances in which the values were equal, and out of the remaining seventy-three pairs, forty-eight, or 66 per cent, in

TABLE 11

Data on the diameter of the entire nerve fibers in μ in larger and smaller rats of the same age—on body weight

AGE	BODY WEIGHT		MEAN DIAMETERS OF ENTIRE FIBERS IN μ							
			First branch		Second branch		Third branch		Fifth nerve	
	Larger rat	Smaller rat	Larger rat	Smaller rat	Larger rat	Smaller rat	Larger rat	Smaller rat	Larger rat	Smaller rat
<i>days</i>	<i>grams</i>	<i>grams</i>								
4	8.5	6.7	3.0	3.0	3.6	3.8	3.7	5.4	5.2	6.2
8	12.8	10.6	3.9	5.4	7.2	5.5	6.6	4.2	6.8	5.5
12	13.5	12.7	5.2	4.7	6.0	5.9	6.4	6.7	6.4	5.9
25	18.9	16.2	6.7	6.4	9.2	8.7	9.5	7.8	10.4	9.2
16	19.6	17.5	6.1	6.0	7.0	6.9	8.6	6.5	7.8	6.8
20	29.3	17.5	7.2	6.7	9.4	7.7	11.6	7.2	11.1	7.9
30	44.0	25.5	8.2	8.3	10.0	8.6	11.3	9.6	10.9	10.1
50	45.0	37.8	8.1	7.7	10.7	9.5	10.9	10.2	12.4	11.1
35	49.5	43.4	7.7	8.3	9.9	10.6	9.3	11.9	11.8	12.8
55	55.3	50.1	9.6	9.4	11.2	10.5	11.2	13.1	11.1	11.2
40	62.0	58.3	9.1	8.9	10.5	10.9	11.4	10.7	14.2	10.1
66	68.2	68.0	9.1	9.1	9.0	10.9	9.0	10.9	11.1	12.8
80	101.9	99.0	9.6	7.7	12.5	11.6	12.0	10.5	13.9	12.4
100	138.0	112.0	9.6	8.9	13.8	12.5	10.3	10.9	15.2	10.9
150	168.7	158.7	9.6	8.3	11.8	12.4	12.4	12.9	12.2	12.7
202	207.9	205.0	10.5	9.6	13.7	11.2	15.6	11.1	15.7	10.6
378	320.0	164.1	11.4	11.6	14.3	11.8	13.1	12.2	14.3	13.3
260	279.5	230.0	12.1	11.4	14.0	15.2	14.0	14.3	13.9	16.8
300	290.0	226.4	12.5	9.5	12.9	12.9	12.5	12.4	13.3	14.8
Averages..	101.8	82.1	8.38	7.88	10.50	9.87	10.49	9.93	11.41	10.53
Ratios.....			1.00 : 0.94		1.00 : 0.95		1.00 : 0.95		1.00 : 0.92	

which the larger diameter of the fibers appeared in the larger animal.

The average values given at the bottom of each column show that in the three branches and in the fifth nerve root the average value of the diameter of the fiber in the larger animals is greater than in the smaller. The smaller animals in these cases have

81 per cent of the larger in body weight, but the diameters of the fibers for the smaller rats, taken from the first branch, have 94 per cent; from the second and from the third branches, 95 per cent, and from the fifth nerve, 92 per cent—thus ranging from 92 to 95 per cent.

If the observations are limited to young animals up to sixty-six days in age, we find in twelve groups the relations shown in table 12.

The comparison between tables 11 and 12 shows that the difference of the body weights given by the smaller and larger is about the same in both tables, and in the younger rats the relative size of the fibers is similar to that found for all ages

TABLE 12

Average values for the diameters of the fibers obtained from young animals of different body weights

	BODY WEIGHT	DIAMETER OF THE ENTIRE FIBER			FIFTH NERVE
		I branch	II branch	III branch	
	<i>grams</i>	μ	μ	μ	μ
Larger rats.....	35.6	6.99	8.64	9.13	9.93
Smaller rats.....	28.7	6.88	8.25	8.68	9.13
Percentage.....	81	96	93	95	91

combined. In general, therefore, the body weight influences the size of the nerve fiber not only in the younger, but also in the more advanced phase of growth.

We consequently conclude that dissimilar body weights at the same age can influence slightly more the growth of the nerve fibers than that of the ganglion cells, but even in the case of the fibers, where the influence is more marked, the response is relatively slight.

THE RELATIVE SIZE OF THE SHEATH AND OF THE AXIS CYLINDER

For this determination thirty-eight rats were used. These were grouped according to the body weights, and the results are given in table 13. The areas of the cross-section of the nerve fibers were found by the usual formula. For each division the

first column shows the areas of the entire cross-section of the fibers, the second column gives the areas for the axis cylinder, while the third column gives the per cent of the total area represented by the axis cylinder. The very last column in the table gives the average of the four values for the percentage area of the axis at each body weight. As these last averages show, the area of the axis is about 44 per cent in the smallest rats examined, but after puberty it rises to about 50 per cent.

TABLE 13

Showing the areas of the fibers and of the axis cylinders in μ^2 in the three branches and in the fifth nerve at different ages—albino rat

MEAN BODY WEIGHT	AGE	FIRST BRANCH			SECOND BRANCH			THIRD BRANCH			FIFTH NERVE			HORI- ZONTAL AVER- AGES
		Entire fiber	Axis	Per cent of axis	Entire fiber	Axis	Per cent of axis	Entire fiber	Axis	Per cent of axis	Entire fiber	Axis	Per cent of axis	
<i>grams</i>	<i>days</i>													<i>per cent</i>
9.7	6.0	11.3	4.5	40	19.6	8.6	44	19.6	8.6	44	27.3	13.5	49	44
16.6	18.0	28.3	12.6	45	42.3	20.1	48	44.2	20.4	46	47.8	22.1	46	46
39.2	36.7	49.0	20.0	41	75.4	33.2	44	89.9	43.0	48	100.8	49.0	48	45
75.8	57.4	63.6	27.3	43	95.0	40.2	42	95.0	44.2	47	109.3	52.8	48	45
140.7	136.9	72.4	33.9	47	120.8	59.4	49	107.7	54.1	50	132.8	72.4	55	50
230.6	298.4	96.8	46.6	48	145.5	80.1	55	139.0	69.4	50	160.6	86.6	53	51
Vertical averages per cent				44			47			48			50	

The vertical averages from the data in table 13 are:

		<i>Range</i>
First branch.....	44 per cent	40 to 48 per cent
Second branch.....	47 per cent	42 to 55 per cent
Third branch.....	48 per cent	44 to 50 per cent
Fifth nerve root.....	50 per cent	46 to 55 per cent

This tabulation suggests that there are local differences in this character, as the average values for the areas increase from the first branch to the trunk and their respective averages correspond in general to the range in the values observed.

The present results agree very well with the previous determinations for the area of the axis as reported by Donaldson ('00)

and Donaldson and Hoke ('05), Dunn ('12), Greenman ('13), and Donaldson and Nagasaka ('18), but are higher than those given by Greenman ('17). These last determinations were made by the planimetric method, while my own determinations as well as all of the others were made by direct micrometric measurements, and this difference in technique may in part explain the difference in the values found.

I should state that in the present study the nerves were fixed with a 1 per cent solution of osmic acid for five days, while all the other authors fixed them for twenty-four hours only. The reason for this difference was that the present author failed to obtain a satisfactory staining after twenty-four hours, and thus a prolongation of the time was necessary. Whether this difference in technique was in any way responsible for slight differences in the results is not clear.

ON THE RELATIVE AREAS OF THE HEAD AND THE RELATIVE AREAS OF THE AXIS CYLINDERS

In regard to the ganglion cells, we have found that the rate of increase in volume corresponds to the rate for the increase in the area of the head surface, so far as the young animals (before eighty days of age) are concerned. It is now of interest to determine what relations hold for the nerve fibers, or, more precisely, for their axis cylinders.

The increase in the area of the axis cylinder in relation to the increase in the surface of the head is shown in table 14.²

The methods of calculating the areas of the axis cylinder, as well as the areas of the head, are the same as those previously employed. The table shows that except in the youngest group the areas of the axis cylinders increase at nearly the same rate as the area of the head surface, i.e., between 16.6 grams in body weight (eighteen days of age) and 230.6 grams in body weight (298 days of age); there is good agreement in five cases. In the first group, however, the ratio of the increase of the area of the

² It must be recognized the head surfaces really innervated by the fifth nerve include not only the skin, with its specialized vibrissae, but also the cavities of the mouth and nose and the teeth. These peculiarities in distribution naturally complicate our problem.

head surface is 1.0:4.56, whereas the mean ratio for the axis cylinders from all three branches is 1.0:9.25.

These differences are possibly due to the fact, as Jackson and Lowrey ('12) stated, that the head has already reached a relatively large size at birth in comparison to the entire body, while the axis cylinders are still immature, and thus the growth rate of these two structures does not coincide. However, after this period of rapid growth of the head area has passed, the ratios

TABLE 14

Showing the relative areas of the heads and the relative areas of the axis cylinders in μ^2 at different ages—albino rats—on increasing weight of head. The grouping of the data in this table is similar to that in table 13, where the body weights and ages for the several groups are given. As the absolute measurements for the areas of the axis cylinders are also given in table 13, they are omitted here, and the ratios alone are presented

RELATIVE AREAS OF HEADS				RELATIVE AREAS OF AXIS CYLINDERS IN SQUARE MICRA			MEAN OF THE THREE BRANCHES	FIFTH NERVE ROOT
Weight of heads				Ratios				
				First branch	Second branch	Third branch		
<i>grams</i>								
$\sqrt[3]{2.2^2}$:	$\sqrt[3]{21.4^2}$:: 1.0 : 4.6	1.0:10.4	1.0:9.3	1.0:8.1	9.3	1.0:6.6
$\sqrt[3]{3.5^2}$:	$\sqrt[3]{21.4^2}$:: 1.0 : 3.3	1.0: 3.7	1.0:4.0	1.0:3.4	3.7	1.0:3.9
$\sqrt[3]{7.1^2}$:	$\sqrt[3]{21.4^2}$:: 1.0 : 2.1	1.0: 2.3	1.0:2.4	1.0:1.6	2.1	1.0:1.8
$\sqrt[3]{9.3^2}$:	$\sqrt[3]{21.4^2}$:: 1.0 : 1.7	1.0: 1.6	1.0:2.0	1.0:1.6	1.7	1.0:1.6
$\sqrt[3]{13.5^2}$:	$\sqrt[3]{21.4^2}$:: 1.0 : 1.4	1.0: 1.4	1.0:1.4	1.0:1.3	1.3	1.0:1.2
$\sqrt[3]{24.4^2}$:	$\sqrt[3]{21.4^2}$:: 1.0 : 1.0	1.0: 1.0	1.0:1.0	1.0:1.0	1.0	1.0:1.0

for the enlargement, both of the areas of the head and the axis cylinder, become more uniform, and in fact after the rat has attained 16.6 grams in body weight (eighteen days of age) approximately similar relations are maintained as far as the observations go. In other words, from eighteen days after birth to 485 days a given area of the head surface is innervated by about the same area of the axis cylinder, but before eighteen days the areas of the fibers increase more rapidly than the area of the head.

THE DIAMETERS OF THE GANGLION CELLS IN RELATION TO THE
DIAMETERS OF THE FIBERS

I wish now to consider the relations between the diameters of the ganglion cells and those of the entire nerve fibers. For this purpose the ganglion cells should be compared with the fibers which belong to the same rat. Such complete data from a single rat were, however, not always available; therefore, I have obtained the approximate corresponding values by the following procedure:

Smooth graphs for the diameters of the cells and of the fibers were drawn on the brain weights corresponding to the observed body weights (Donaldson, '15), and from the graphs thus drawn the missing values for the diameters of the cells or of the fibers, respectively, were read. The data so obtained were then tabulated in detail.

In order to see more clearly the relation between the ganglion cells and the nerve fibers, table 15 was prepared from these detailed data. In table 15 the entire data were arranged in nine groups, which enable one to compare the average diameters of the largest nerve cells in the gasserian ganglion with the corresponding average diameters of the largest myelinated fibers, or their axis cylinders, arising from them, taken from the first, second, and third branches and from the fifth nerve root.

Looking at the series of ratios at the bottom of table 15 showing the increase in the diameters of the cells as compared with those of the fibers, it appears that while the cells increase 1.39 times, the four sets of fibers have increased between 2.78 and 2.05 times, while the increase in the axis cylinders is greater in general than that for the entire fibers, ranging from 3 to 2.41 times.

To illustrate the changes in the ratios from the first to the last group in table 15 we have made table 16, giving for each branch and for the fifth nerve root the ratios obtained by dividing the diameters of the cells by the diameters of the respective nerve fibers. This table shows that the ratios decrease in general from the first to the last groups, and this result is merely a consequence of the fact that the fibers are growing in diameter more

rapidly than the cell bodies. Indeed, we have already seen that the cells have almost ceased to grow at puberty, while some slight growth is still shown by the fibers.

The increase in the axis cylinders is somewhat more rapid than that for the entire fiber, and hence for them the final ratios would be even smaller. The ratios of the ratios at the bottom

TABLE 15

Showing the relation between the diameters of the cell bodies and of the fibers in rats at different ages. The series of values under the diameters of the entire fibers are for the diameters of the corresponding axes

NUMBER OF ANIMALS USED	RANGE IN BODY WEIGHT	MEAN BODY WEIGHT	AVER- AGE AGE	BRAIN WEIGHT	DIAMETERS					
					Cell body	Nu- cleus	First branch	Second branch	Third branch	Fifth nerve
	<i>grams</i>	<i>grams</i>	<i>days</i>	<i>grams</i>	μ	μ	μ	μ	μ	μ
6	6.7- 13.1	10.9	7.4	0.755	35.5	14.8	4.2	5.5	5.3	7.0
							2.7	3.6	3.9	4.1
8	13.5- 29.3	17.6	17.8	1.095	38.9	15.6	6.3	8.0	7.9	8.4
							4.2	5.4	5.3	5.7
8	21.0- 29.3	23.5	21.0	1.225	41.8	15.3	7.3	8.1	9.5	9.3
							4.8	5.3	6.3	6.0
10	33.1- 46.0	39.9	37.5	1.412	43.1	15.8	7.9	10.0	10.9	11.5
							5.0	6.7	7.7	8.3
10	49.5- 76.1	63.7	52.2	1.552	46.4	16.0	9.0	11.0	10.6	12.0
							5.8	7.3	7.4	8.2
6	96.9-138.0	110.6	84.2	1.708	48.9	16.3	8.8	12.5	10.8	12.7
							6.0	8.6	7.4	9.3
8	150.0-195.5	172.6	176.3	1.826	49.4	16.1	9.5	12.3	12.7	12.6
							6.6	8.4	9.3	9.4
8	202.6-245.5	217.5	230.0	1.888	48.2	16.1	10.3	13.2	13.4	14.1
							7.5	10.0	9.8	11.1
7	254.6-339.0	291.4	341.7	1.949	48.2	16.3	11.7	14.2	13.5	14.4
							8.1	10.6	9.4	11.8
Ratios.....					1:1.39	1:1.10	1:2.78	1:2.58	1:2.54	1:2.05
Axis cylinder.....							1:3.00	1:2.94	1:2.41	1:2.87

of table 16 simply serve to indicate that the growth of the fibers in diameter is somewhat less rapid in the case of the fifth nerve root than in the branches.

THE MORPHOLOGICAL CHANGES IN THE GANGLION CELLS DURING GROWTH

Using the material prepared for the present study, I have also noted some of the morphological changes in the ganglion cells, but since cytological studies were not originally planned, my present observations are necessarily restricted.

TABLE 16

Based on table 15. Giving the ratios of the diameters of the nerve fibers in the several branches and in the fifth nerve to the diameter of the nerve cells. The body weights and ages for the nine groups here entered are given in table 15

GROUP	I BRANCH : G. G. FIBERS CELLS	II BRANCH : G. G. FIBERS CELLS	III BRANCH : G. G. FIBERS CELLS	FIFTH NERVE ROOT FIBERS : G. G. CELLS
1	1:8.5	1:6.5	1:6.7	1:5.1
2	1:6.2	1:4.9	1:4.9	1:4.6
3	1:5.7	1:5.2	1:4.4	1:4.5
4	1:5.5	1:4.3	1:4.0	1:3.8
5	1:5.2	1:4.2	1:4.4	1:3.9
6	1:5.2	1:3.9	1:4.6	1:3.8
7	1:5.2	1:4.0	1:3.9	1:3.9
8	1:4.7	1:3.7	1:3.6	1:3.4
9	1:4.1	1:3.4	1:3.6	1:3.4
Ratio of ratios 1-9.....	1:0.48	1:0.52	1:0.54	1:0.67

Plate 1 illustrates in semidiagrammatic form the larger cells in the gasserian ganglion of the albino rat at birth and at 20, 100, and 485 days. The cells were enlarged proportionately to the values of the diameters given in table 3.

The cell body of the ganglion cells is relatively small at birth (figs. 1 to 3), but the Nissl bodies are already well differentiated. Such well-differentiated Nissl granules are also found in the cells of intermediate and small size at this age, and well-developed Nissl bodies may be seen even in the dendrites. However, during this early period the Nissl bodies appear to be less abundant and

smaller in size than they are later. The nucleus, on the other hand, is already large at birth and the chromatin well differentiated.

The so-called 'kernfaden' are to be seen very often. In the next period at twenty days (figs. 4 to 6) the increase in the cell body is much more rapid than the increase of the nucleus and the Nissl bodies have increased not only in number, but in size also. At this period the sections stain a deep violet or blue, instead of a light violet, which color was common in the younger material. This change in reaction appears not only in the Nissl granules, but also in the ground substance of both the cytoplasm and the nucleus. These changes are to be seen in the intermediate and in the smaller cells also which are found everywhere at this age. The interstitial tissues of the ganglion are seen to be well developed, but are still immature, as can be told from the well-stained nuclei and scantiness of the fiber substance. Owing to the paucity of the interstitial tissue, the ganglion cells are rather closely packed.

The nucleus attains nearly its maximum size at the age of about thirty-five days, as stated earlier. In this period no special morphological changes of note were to be found either in the cell body or in the nucleus, with the exception of the increase in the size of the cell body and the nucleus.

It should, however, be stated that there occur gradual and progressive changes in all structures, such as a slightly deeper stain of the Nissl bodies, the ground substance of cytoplasm, etc., but no sharp lines can be drawn between the ages of twenty and 485 days (figs. 4 to 12).

Nissl ('94, '95), Lugaro ('96), Lenhossek ('97), Cox ('98), Hatai ('01), and others have discussed the arrangement of the stainable substance in the spinal ganglion cells according to the size of the cell body, and I have attempted to classify various forms of the ganglion cells in the gasserian ganglion by the same method.

My own observations do not agree entirely with the description given by the authors just mentioned, but I am not ready to discuss the matter at this moment, because my observations

are not sufficiently extensive. However, I can distinguish three types of ganglion cells, as was noted by Hatai, for the spinal ganglion cell in the albino rat.

As shown in plate 1, the largest cells in all the four age groups show the following arrangements of the stainable substance.

A. The cells with large, coarse, stainable masses which lie throughout the cell body without showing a regular or constant arrangement (figs. 2, 5, 8, 11).

B. The cells with large, coarse, stainable masses only at the periphery. Smaller masses fill up the remaining part (figs. 3, 6, 9, 12).

C. The cells with large, coarse, stainable masses which lie throughout the cell body, showing a regular, concentric arrangement (figs. 1, 4, 7, 10).

In all these cells clear spaces around the nucleus and at the extreme periphery of the cell body are distinctly visible.

The small cells and those intermediate in size show at each age a somewhat similar distribution of the stainable substance, but tend to differ from the largest cells by having the clear zones less sharply marked and by a tendency to shrink, which is most marked in those of smallest size.

Thus the morphological characters of the cells which compose the gasserian ganglion are similar to those shown by the cells of the spinal ganglion.

ON THE RELATIONS BETWEEN THE GROWTH OF THE GANGLION CELLS AND THE NERVE FIBERS AND THAT OF THE TEETH

Since the fifth nerve supplies its branches not only to both maxillaries, but also to the teeth, it is conceivable that the cells and fibers of the gasserian ganglia might be correlated in their growth with that of the dental mechanism. I have endeavored to determine whether or not such a relation exists.

Addison and Appleton ('15, pp. 91-93) studied the growth of the incisors of the albino rat and found that "In animals one day old the upper and lower incisor teeth measure 2.3 and 3 mm., respectively. At 8 to 10 days these teeth erupt, and at 10 days measure 7 and 11 mm. respectively. This period is therefore characterized by the rapid elongation of the teeth. The process

of attrition begins within a few days after eruption, so that by 19 or 21 days of age, the typical occlusal surface is formed."

"At 21 and 23 days the first two molars erupt in both upper and lower jaws, and from now on the animal is able to secure food for itself, and if necessary can maintain an independent existence. The third molars are delayed until two weeks later and do not appear until about the 35th day."

In table 17 the first two columns are supplementary to the table given by Addison and Appleton.

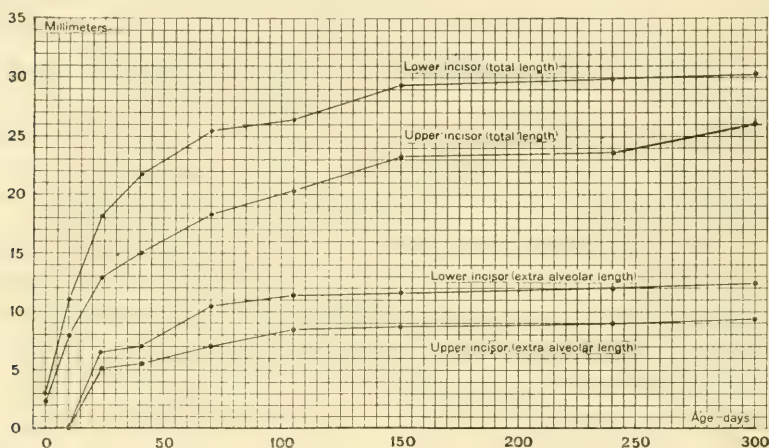


Chart 5 Based on table 17 and giving in millimeters on age the total and the extra alveolar lengths of the lower and upper incisors.

Chart 5 shows graphically the relations of the data given in table 17. The ordinate values represent total length and the extra alveolar length, respectively, of the upper and the lower incisors on age. In the graphs we can distinguish clearly three phases of growth, namely, 1) the period of the rapid elongation of the teeth, which extends from birth to 23 days; 2) the period of the slow elongation which extends from 23 to 105 days, and, 3) the period of still slower elongation which extends from 105 days to 10 months after birth.

We have noticed already that the myelination of the axis is distinct at twelve days and about this time (eight to ten days)

the eruption of the incisors occurs. Again, at about twenty days, the growth of the ganglion cells, the nuclei, and the nerves reach the end of their first phase, coinciding with the end of the first phase of the growth of the incisors.

The period at which the third molar erupts corresponds to the period of nearly the full size of the nucleus, i.e., about thirty-five days. We notice, moreover, that the period at which the cell body, nucleus, and the fiber reach nearly the maximum is ninety days, but the extra alveolar length of the incisors attains nearly its maximum a trifle later—105 days—after which it increases slowly. Thus the fuller growth of the nerve elements

TABLE 17

Measurements on the incisor teeth in millimeters, on age

	AGE IN DAYS								
	1	10	23	41	70	105	150	240	300
Upper incisor total length.....	2.3	7.9	12.8	15.0	18.3	20.3	23.3	23.7	26.2
Upper incisor extra alveolar length.....	Eruption 8-10 days		5.1	5.5	7.0	8.4	8.7	9.0	9.3
Lower incisor total length.....	3.0	11.0	18.1	21.7	25.5	26.4	29.4	29.9	31.3
Lower incisor extra alveolar length.....	Eruption 8-10 days		6.5	7.0	10.5	11.4	11.6	12.0	12.4

seems to be slightly in advance of that of the dental mechanism, yet in general there is a fairly good correlation between them.

ON THE RELATION BETWEEN THE GROWTH OF THE GANGLION CELLS AND THE NERVE FIBERS AND THAT OF THE CRANIUM

Recently Donaldson ('19) studied the growth of the entire skeleton, as well as its several parts, in the albino rat. So far as his results on the cranium are concerned, the rate of growth with respect to age coincides very well with the growth rate of the ganglion cells and the fibers of the fifth nerve.

For instance, the rapid growing period of the cranium continues up to about twenty days and the next period of the slower growth

up to 100 days, and finally the period of the very slow growth follows and continues up to 485 grams in body weight.

The percentage of water in the skeleton shows also a close agreement with the growth phases of the ganglion cells and the fibers.

From these resemblances in the manner of maturation of these various characters—teeth, cranium, and gasserian ganglion cells and fibers—the following brief statement may be made.

From eight to ten days after birth the incisors of the upper and lower jaws erupt and shortly after that (about twelve days) the myelination of the nerve fibers becomes evident. From twenty to twenty-three days of age the molars in both the upper and lower jaws erupt, the incisors are already well elongated and the rat is able to maintain an independent existence.

Before weaning the gnawing apparatus must be adequate, and indeed we notice that the cranium is well developed not only in size and weight, but, as is indicated by the loss of water, the solidity of the cranium becomes adequate to give firm support to the teeth and to resist the strain produced during the gnawing. For an adequate supply of the nerves to these organs, the cell body increases in volume very rapidly, and at the weaning time the cell body and the nucleus have already reached the appearance which they have in the adult rat. The nerve fibers also approximate in area those found in the adult. At about thirty-five days of age the third molars erupt in both the upper and lower jaws and at the same time the ganglion cells have become considerably larger, and at puberty or earlier, all the organs above described show full development.

COMPARISON OF THE MEASUREMENTS ON THE NEURONS OF THE
FIFTH CRANIAL NERVE WITH THOSE MADE ON THE
SEVENTH CERVICAL SPINAL NERVE BY
DONALDSON AND NAGASAKA ('18)

It was one purpose of the present study to determine whether the size and growth of the neurons in the gasserian ganglion was like that found in a typical spinal nerve or, if not, to indicate the differences observed. As both sets of specimens were prepared by the same technical methods, the values may be directly compared.

1. *Absolute size at maturity*

Diameters of cells and nuclei, table 18, have been based on the average for the computed diameters of the last two entries in the foregoing table 3—for the cells in the gasserian ganglion and for the cells of the seventh cervical ganglion—on the average of the last three entries (in table 3, loc. cit.).

TABLE 18
Computed diameters of mature cells

GASSERIAN GANGLION			SEVENTH CERVICAL GANGLION		
Body weight	Cells	Nuclei	Cells	Nuclei	Body weight
<i>grams</i>					<i>grams</i>
263	48.4 μ	16.8 μ	38.1 μ	18.0 μ	264

The values just given show that when compared with the cells of a spinal ganglion the largest cells of the gasserian ganglion have a greater diameter, but the diameter of their nuclei is less than those in the spinal ganglion cells. The nucleus-plasma ratio must therefore be greater for the gasserian cells. Using the foregoing values, these ratios stand as in table 19.

TABLE 19
Nucleus-plasma ratio

GASSERIAN CELLS		SPINAL GANGLION CELLS	
Nucleus	Cell	Nucleus	Cell
1:22.9		1:8.5	

We note here that a low nucleus-plasma ratio is characteristic for cells which have not completed their growth.

Turning to the fibers, we may compare the average diameters of the entire fibers and their axes in the root of the fifth cranial nerve (average of last three entries in table 10) with the corresponding measurements on the dorsal root fibers of the seventh cervical spinal nerve (average of last three entries in table 2, loc. cit.).

The data in table 20 show that the fibers and axes in the root of the fifth nerve are smaller in diameter than the corresponding fibers in the dorsal root of the seventh cervical spinal nerve.

Further, the fibers in the ramus ophthalmicus have a less diameter than the largest fibers in the nerve root. If the fibers in the seventh nerve (last column in table 20) are compared with the corresponding root fibers, they are also a trifle smaller, but on the other hand they are much larger in diameter than those of the ramus ophthalmicus. Among these data the fairest comparison can be made between the fibers from the respective dorsal roots, and this shows the fibers in the dorsal root of the fifth nerve to be much less in diameter than the corresponding fibers for the dorsal root of the seventh cervical nerve, despite the fact

TABLE 20

Diameters of nerve fibers in the fifth cranial and seventh cervical spinal nerves

ROOT OF FIFTH NERVE			RAMUS OPHTHALMICUS		DORSAL NERVE ROOT		SEVENTH NERVE		
Body weight	Fibers	Axes	Fibers	Axes	Fibers	Axes	Fibers	Axes	Body weight
<i>grams</i>									<i>grams</i>
251	14.4 μ	10.5 μ	11.4 μ	7.8 μ	18.3 μ	13.4 μ	18.1 μ	13.1 μ	264

that the cells of the gasserian ganglion have the greater diameter and a much higher nucleus-plasma ratio.

If we turn now to the growth changes in the cells forming the two ganglia under discussion, the differences will be most readily brought out by contrasting the amount of growth after puberty. For this we have taken the values at about 80 grams of body weight, using for the gasserian ganglion the data at 85 grams of body weight (table 3) and for the spinal ganglion the data at 81 grams (table 3, loc. cit.).

Table 21 clearly indicates that between 80 grams of body weight, or just before puberty, and the end of our record there is but very slight growth in the diameter of the cell body or nucleus of the elements in the gasserian ganglion, while the neurons in the seventh cervical ganglion grow very markedly.

It follows from this that the gasserian ganglion differs from a spinal ganglion by the fact that the cell bodies composing it have nearly completed their growth at puberty, while in the spinal ganglion growth is much more prolonged.

If a similar comparison is made to show the growth of the fibers, it seems best to use those appearing in the respective dorsal roots.

The data for the sensory root of the fifth nerve are based on the average (84 grams) of the two sets of values at 68 and 100

TABLE 21

Growth in diameter of cell bodies. This table to be read vertically

GASSERIAN GANGLION			SPINAL GANGLION		
Body weight	Cell	Nucleus	Cell	Nucleus	Body weight
<i>grams</i>					<i>grams</i>
85	46.6 μ	16.5 μ	29.4 μ	15.2 μ	81
263	48.4 μ	16.8 μ	38.1 μ	18.0 μ	264
Gain	+4%	+2%	+29%	+18%	Gain

TABLE 22

On the growth of the nerve fibers and their axes in diameter. This table to be read vertically

ROOT OF FIFTH NERVE			SEVENTH CERVICAL DORSAL ROOT		
Body weight	Fibers	Axes	Fibers	Axes	Body weight
<i>grams</i>					<i>grams</i>
84	12.6 μ	8.9 μ	13.2 μ	7.8 μ	81
251	14.4 μ	10.5 μ	18.3 μ	13.4 μ	264
Gain	+14%	+18%	+39%	+72%	Gain

grams of body weight as given in table 10, and for the sensory root of the seventh cervical nerve on the values at 81 grams of body weight (table 2, loc. cit.). The relations are shown in table 22.

Here, as in the case of the cell bodies, the growth of the fibers in the sensory root of the seventh cervical is more marked.

The foregoing comparison enables us to contrast the growth and size of the two sets of neurons under consideration. More

observations on other spinal ganglia and on the ganglia of the several cranial nerves are needed before any general conclusions can be drawn, but if we use the present observations and take the seventh cervical ganglion as the standard, it appears that the gasserian ganglion is characterized by larger cells, smaller nuclei, and a higher nucleus-plasma ratio, while the fibers forming the sensory root are smaller, though the axis sheath relation is the same in both.

When growth after 80 grams of body weight, i.e., after puberty, is considered, it appears that the growth of the cells comes nearly to a standstill at puberty, though the fibers continue to increase in diameter to a slight extent.

It seems possible from these relations that the neurons in the more specialized cranial ganglia mature earlier than do those in the spinal ganglia.

SUMMARY

The measurements were made on twenty-five of the largest ganglion cells in seventy-six gasserian ganglia taken from thirty-eight normal albino rats, and on the ten largest fibers from the first, the second, the third branch, and the fifth nerve root in thirty-nine albino rats.

For the fixation of the cells Bouin's fluid was used, and for the fibers one per cent osmic acid.

From these data the following results were obtained:

1. The growth of the ganglion cells shows three distinct phases: 1) a rapid growing period which extends from birth to about 20 days; 2) a slower growing period which covers from about 20 to about 80 to 100 days; 3) finally, a period of much slower rate (or even a slight atrophy) which extends to the end of the observations, or 485 days. The growth of the nucleus shows phases similar to those for the cell bodies.
2. The nuclei are relatively well developed at birth and their increase in diameter is slower than that of the cell body.
3. Among rats of the same age those with heavier body weights have larger cell bodies, nuclei, and fibers than those which are smaller. This influence of the body weight on these structures

is about the same in the younger and in the older rats. The amount of the difference is, however, small.

4. So far as the diameters of the cell body, the nucleus, and the fibers are concerned, the difference between those from the left and those from the right side is negligible.

5. The ratios between the volumes of the cytoplasm and the volumes of the nuclei increase with increasing size (age) of the ganglion cells, and the largest cells give a ratio over twice as large as that found in the smallest.

6. At about twenty days after birth the cell body and the nucleus show almost the same appearance as that in the adult rat. After twenty days both increase in size, and there is also an increase in the quantity of the Nissl substance, but the other changes of a morphological character are very slight.

7. The diameter of the fibers is least in the first branch (ophthalmic) and largest in the fifth nerve root, while the fibers of the second (maxillary) and the third (mandibular) branches are similar and give intermediate values.

8. The relative area of the axis cylinder to that of the entire fiber increases slightly with age, and approximates the one-to-one relation in the nerve fibers of the adult rat.

9. The volume of the ganglion cells increases at the same rate as the area of the head surface in the younger animals, before eighty days of age; but after this age the growth of the neurons becomes very slow, while the growth of the head continues.

10. After about eighteen days of age the areas of the axis cylinders of the fifth nerve increase at about the same rate as the area of the head; previous to this age the growth in the area of the head has been the more rapid.

11. The ratios given by the diameters of the ganglion cells to the diameters of the nerve fibers decrease with increasing body weight. The decrease of the ratios after puberty is due to a longer continued growth in diameter of the fiber as compared with that of the ganglion cells.

12. The neurons in the gasserian ganglion are larger, have a higher nucleus-plasma ratio, and mature earlier than do those in the ganglion of the seventh cervical nerve. The fibers from

the cells of the gasserian ganglion are absolutely less in diameter than those of the seventh cervical ganglion, despite the fact that the cell bodies of the former are larger. These differences may be related to the somewhat specialized character of the fifth cranial nerve.

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PLATE 1

EXPLANATION OF FIGURES

1 to 12 Showing in a semidiagrammatic way the three arrangements of the stainable substance in four age groups of the largest cells in the gasserian ganglion of the albino rat.

Arrangement A in figures 2, 5, 8, 11.

Arrangement B in figures 3, 6, 9, 12.

Arrangement C in figures 1, 4, 7, 10.

Enlargement, $\times 600$.

1 day



1

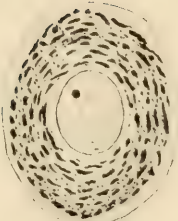


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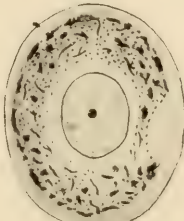


3

20 days



4

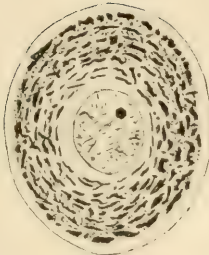


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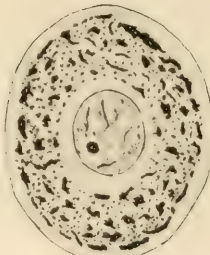


6

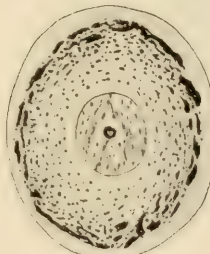
100 days



7



8



9

485 days



10



11



12

Resumen por el autor, Davidson Black,
Peking Union Medical College, Peking, China.

Estudios sobre la anatomía endocraneal.

II. Sobre la anatomía endocraneal de *Oreodon* (*Merycoidodon*).

El autor trata brevemente de la importancia de los vaciados endocraneales en la interpretación de la morfología del cerebro de los mamíferos vivientes y extinguidos, volviendo a indicar las diferencias entre los vaciados endodurales y endocraneales. En el presente trabajo estudia con detalle la morfología de cinco moldes endocraneales naturales de *Oreodon* (*Merycoidodon*) *culbertsonii* Leidy, así como un vaciado endocraneal obtenido con escayola en la región cerebelar de uno de los ejemplares. Una rica serie de datos sobre la morfología cerebral y cerebelar se ha conservado en estos moldes y gracias a ella ha sido posible restaurar gráficamente el cerebro de *Oreodon*.

El autor estudia sucesivamente las medidas de los ejemplares, la irrigación sanguínea endocraneal, los orificios endocraneales, rinencéfalo, neopallium y cerebelo, suministrando pruebas que indican que la expansión de la proyección visual y, especialmente, la auditiva y áreas primarias de asociación del neopallium han progresado en grado considerable, mientras que en apariencia no sucede lo mismo con la corteza en las proximidades de las áreas somática sensorial y área de proyección motriz, situadas frontalmente. El cerebelo, sin embargo, presenta tan alto grado de especialización en ciertos aspectos, de ningún modo inferiores y en grado considerable idénticos a los de los modernos artiodáctilos, que la presencia de un centro de proyección activo y funcional en el neopallium debe considerarse como un postulado.

Los caracteres endocraneales de *Oreodon* son semejantes a los pertenecientes a un artiodáctilo macrosmático primitivo, aun cuando existen otros rasgos más determinados que aunque confirman su naturaleza artiodáctila hacen su posición dentro del orden difícil de definir.

STUDIES ON ENDOCRANIAL ANATOMY

II. ON THE ENDOCRANIAL ANATOMY OF OREODON (MERYCOIDODON)

DAVIDSON BLACK

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FORTY-EIGHT FIGURES

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INTRODUCTORY

The material on which this study is based was obtained through the courtesy of Professor H. F. Osborn and Dr. W. D. Matthew and is a part of the Exchange Palaeontological Collection presented by the American Museum of Natural History to the Museum of the Department of Anatomy of the Peking Union Medical College.

The extinct artiodactyl ungulates comprising the family Oreodontidae were primitive ruminants presenting such a peculiar admixture of characters as to induce Leidy to refer to them as ruminating hogs (v. Leidy, 20, and Scott, 28, p. 372). These animals were restricted in their distribution to North America where their remains have been found in large numbers in the middle Tertiary deposits of that continent.

Many genera of this family have been distinguished ranging in time from upper Eocene to lower Pliocene. The specimens here described are all of Middle Oligocene age and were taken in the Oreodon Zone of the White River Group of the Big Bad Lands in South Dakota (v. Osborn, 24, map and sections, figs. 20 and 22).

Two of the specimens, numbers II and IV respectively, were identified as *Oreodon culbertsonii*, Leidy, which by right of priority should read *Merycoidodon culbertsonii*, Leidy.¹ The other specimens labeled *Oreodon* are also of the genus *Merycoidodon*.

Of the five natural casts here described, specimen I was already prepared for study when it came into my hands. The technical work in connection with the preparation of the other specimens has been done in the Anatomical Laboratory of this institution.

The natural endocranial cast of *Oreodon* has been previously figured and briefly described by Leidy (21, pp. 14, fig. 11) but unfortunately this paper is not accessible to me. It is desirable, however, that a further study be made of this interesting material.

¹ In his original description of this genus Leidy (20) made use of the name *Merycoidodon*, though it was subsequently discarded by him and by many succeeding writers in favor of the name *Oreodon* (vide Hay, 17).

A short preliminary report has already been made with this in view (3) though at that time but two of the specimens had been examined in detail.

Moodie (22, fig. 14) has figured a ventral view of an endocranial cast of *Merycoidodon culbertsonii*, Leidy, in connection with his annotations on the subject of Tertiary mammalian brain casts. His specimen was evidently very badly weathered. Outline drawings of the endocranial cast of an oreodont, *Merycochoerus*, have also been published by this author (23, figs. 2 and 3). No description, however, is given of this cast and his terminology in labeling the endocranial detail in the figures is difficult to interpret.

In the introduction of his earlier publication this author makes the following statement with regard to brain casts in general: "The cast in either case" (reptiles or mammals) "is of the dural cavity and gives only an approximate picture of the actual configuration of the brain of the animal, whether reptile or mammal, since the smaller convolutions make no impression of the inner surface of the skull, even in man" (22, p. 136). This statement seems to have been made on the strength of Scott's earlier work (27) but does not at all coincide with my own observations.²

In order to be sure how much information about the morphology of the brain of fossil mammals might safely be deduced from a study of endocranial casts, I undertook some years ago to make a series of endodural, endocranial and encephalic casts of recent forms for comparison. A considerable number of such casts were prepared, the material used being chiefly *Canis familiaris* and *Felis domestica* but other material was also employed (*Ovis*, *Sus*, *Bos*, *Viverra*, *Putorius*, etc.).

As a result of these comparisons it became quite evident that in the adult animals investigated, practically all the details of the pattern of the lateral convex surface of the cerebrum were

² With reference to this question Elliot Smith (12, q. v.) pointed out long ago that accurate information concerning the brain could be gleaned from the study of casts of the cranial cavity in the case of most of the lower gyrencephalous mammals.

recorded on the endocranial casts with certain additions, viz.: 1) the course of the meningeal vessels is usually reproduced with minute detail; and 2) the grooves for the superior sagittal sinus and its chief tributaries are evident, and by reason of the absence of the falx cerebri the mesial boundary of the cerebral hemispheres is not defined. On the adult cerebrum in no cases were small sulci present that did not leave some impression (frequently quite sharply defined) upon the corresponding endocranial surface of the bone. This, however, was not always the case in immature individuals.

In adult carnivore skulls, especially in males, a considerable amount of tentorial ossification occurs which increases with age. Where the ossification is extensive the tentorium osseum retains imprinted upon it the details of the fissural pattern of the tentorial surface of the cerebrum as well as that of the cerebellum. In such specimens it was possible by casting separate cerebral and cerebellar portions, or by breaking the cast along the tentorial plane, to obtain accurate information of the morphology of the adjacent parts.

In view of the greater minutiae of its detail, the cerebellar morphology is usually not reproduced so clearly in an endocranial cast as that of the cerebrum. The most important landmarks of cerebellar morphology are, however, as a rule preserved.

In contrast to endocranial casts, those of the endodural cavity do not exhibit such sharpness of detail, and of course never show any indication of the course of the meningeal vessels nor of the grooves and vacuities for the venous sinuses. On the other hand, the salient features of cerebral configuration along the line of the great sagittal fissure are preserved and the line of demarcation between cerebrum and cerebellum is sharply defined by the tentorium while in their general proportion and measurements the casts more nearly accord with those of the corresponding brains. It is thus possible to distinguish endocranial and endodural casts with no possibility of confusion.

It is evident that no cast can be one of the dural cavity which shows upon its surface the detail of meningeal vessels, and irregularities corresponding to apertures such as the parieto-temporal

canal. If a cast be endodural (i. e., a cast of the cavity enclosed by the dural sheath) there can be no trace on it of a sagittal skull groove for the lodgement of the superior sagittal sinus, but in its place will be found a cleft corresponding to the falx and reproducing the great sagittal fissure and incidentally the margo medialis cerebri. It follows, therefore, that the casts described in this paper and all others formed in like manner by the displacement of the soft parts within the skull by mineral debris, are natural endocranial casts.

Notwithstanding the fidelity of detail with which the cerebral fissural pattern of the lower gyrencephalous mammals is reproduced upon their endocranial casts, the interpretation of this pattern is frequently a matter of considerable difficulty. This must be in the nature of the case, especially when the secondary sulci are richly developed, since even in the examination of the brain itself in well known modern forms it becomes necessary to open up the fissures in many cases before the certain interpretation of their arrangement and homology is possible.

In concluding these general remarks, comment may be made on the significance of the fact that in all the Anthropoidea and especially in man the convolutions and sulci over the convex surface of the cerebrum are poorly reproduced on the endocranial skull surface. In man only on the skull parts abutting upon the orbital and inferior temporal surfaces of the cerebrum, and to a lesser extent on the occipital surface, is the cerebral pattern defined with a sharpness comparable with that obtaining over the whole cerebral endocranial surface in the dog. This, however, is not the case among the Prosimii.

The probable explanation of this phenomenon is to be looked for in the comparatively recent origin of the members of the group Anthropoidea, together with the fact that this order as a whole is characterized by the elaboration of certain phylogenetically new neopallial areas which made their appearance in the frontal and temporo-parietal regions and show a gradual increase in their differentiation and expansion as one ascends the anthropoid scale. The relative length of time during ontogeny in which the cerebrum continues to expand and differentiate is greater

among the Anthropoidea than in other mammalian orders and greatest in man in whom postnatal brain growth and differentiation is continued for many years.

I have elsewhere observed (1) that one of the most important conditions contributing to the endocranial reproduction of cerebral pattern lies in the early maturation of growth processes in the encephalic portion of the skull. Since this condition is less nearly fulfilled in man than in any other mammalian form, it is to be expected that the human *juga cerebralia* and *impressiones digitatae* will be correspondingly poorly developed. Conversely with but few exceptions one may look for close endocranial and encephalic correspondence in gyrencephalous mammalian types below the anthropoidean scale, and even within the latter group in the less generalized primitive extinct forms.

DESCRIPTION OF SPECIMENS

Specimen I (figures 1 to 4 and 27 to 30)

The cerebral portion only of the endocranial cast is represented, so that nothing can be learned of the structures which occupied the olfactory skull fossae nor of those situated below the plane of the tentorium in this specimen.

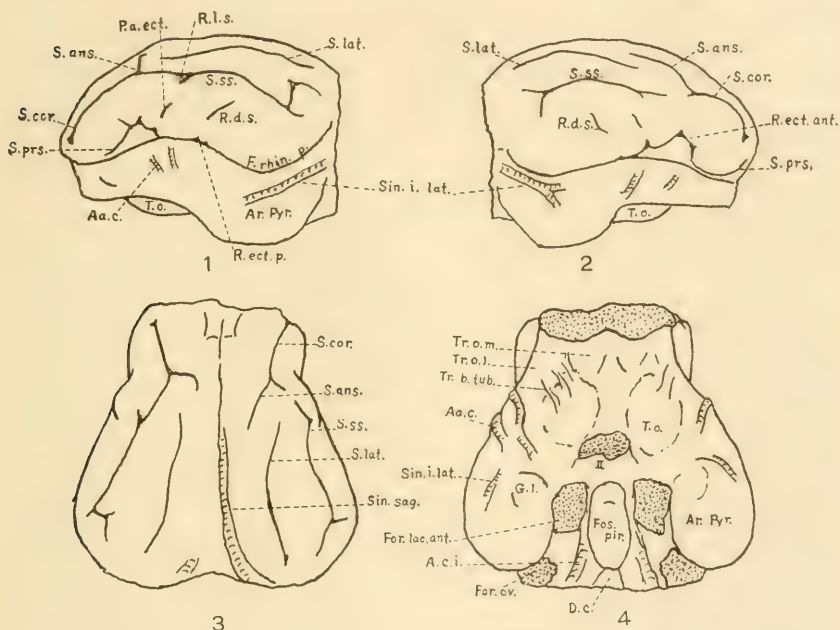
The transverse diameter of the cast is greatest in its posterior third, dorsal to the groove corresponding to the rhinal fissure, where it measures 4.3 cm. The maximum transverse diameter between the eminences corresponding to the pyriform lobes is 4.1 cm. From the frontal to the occipital pole of the cast the maximum length is 4.1 cm. and the maximum height is 3.0 cm. The volume of the cast is 28 cc.³

Basis cerebri. (Fig. 4.) On the basal surface the relation of the diverging medial and lateral olfactory tracts to the prominent protuberance of the *bulbus olfactorius* and to the pyriform lobe, is clearly indicated on both right and left sides of the cast.⁴ In

³ In this and succeeding specimens the volume was determined by the water displacement method so these figures can only be considered as approximate. The linear measurements are all taken to the nearest tenth.

⁴ For convenience throughout this description many of the surface markings which of course are all the result of moulding of the natural cast by endocranial structures, will be referred to as parts of the central nervous system.

addition, there may be seen on both sides, but particularly on the right, several strand-like markings extending in graceful curves from the surface of the lateral olfactory tract to that of the tuberculum olfactorium. These markings which strongly recall the picture of this region in the highly macrosomatic brain



Figs. 1, 2, 3 and 4 Camera lucida drawing of natural endocranial cast of Oreodon, Specimen I, left lateral, right lateral, dorsal and ventral views respectively. For photographs see figures 27 to 30. Abbreviations: *A.a.c.*, ridges corresponding to middle cerebral arteries; *A.c.i.*, internal carotid artery ridges; *Ar.Pyr.*, caudal expansion of pyriform lobe; *D.c.*, depression for lodgment of posterior clinoid processes; *F.rhin.p.*, posterior rhinal fissure; *For.lac.ant.*, broken surface corresponding to anterior lacerated foramen; *For.ov.*, broken surface corresponding to foramen ovale; *Fos.pit.*, eminence corresponding to pituitary fossa; *G.l.*, gyrus lunaris of Retzius; *P.a.ect.*, processus acuminis ectosylvii; *R.d.s.*, ramus descendens suprasylvii; *R.ect.ant.*, ramus anterior ectosylvii; *R.l.s.*, ramus lateralis suprasylvii; *S.ans.*, ansate sulcus; *S.cor.*, coronal sulcus; *S.lat.*, lateral sulcus; *S.prs.*, presylvian sulcus; *S.ss.*, supra-sylvian sulcus; *Sin.i.lat.*, infero-lateral sinus; *Sin.sag.*, sagittal sinus; *T.o.*, tuberculum olfactorium; *Tr.b.tub.*, tractus bulbo-tubercularis; *Tr.o.l.*, lateral olfactory tract; *Tr.o.m.*, medial olfactory tract; *II*, chiasma ridge.

of *Orycteropus* (v. Elliot Smith, 13, fig. 1) may well correspond to grooves for the lodgement of a highly developed tractus bulbotuberculare, and as such they have been labeled in figure 4.

The small area corresponding to the locus perforatus anticus, situated lateral to the chiasma ridge and between the protuberance of the olfactory tubercle and that of the caudal end of the pyriform lobe, is obscured on both sides by indistinct and irregular markings which are evidently of vascular origin. The pyriform lobes are large and prominent, and in shape and proportions again recall the conditions obtaining among modern Edentates in the highly macrosomatic brain of *Orycteropus* (vide 11 et infra).

In proportion to the size of the olfactory roots, the optic tracts are small. The chiasma ridge is depressed and the optic nerves at the point of their emergence from the endocranium do not appear to be separated from one another by a bony lamina.

As is usual among artiodactyls the foramen lacerum anterius affords passage for both ophthalmic and maxillary divisions of the trigeminus and the mandibular division of this nerve makes its exit from the skull by way of the foramen ovale. In proportion to the size of the cast these roots are very large.

The pituitary fossa is represented by an elongated, oval, azygos protuberance whose indistinct rostral boundary is indicated by a shallow depression a short distance caudal of the chiasma ridge. A sharply marked but shallow depression corresponding to the posterior clinoid processes forms the caudal limit of this area.

On each side between the pituitary protuberance and the elevation corresponding to the ophthalmic-maxillary division of nerve V, are narrow but well marked longitudinal ridges which represent skull grooves for the lodgement of the small internal carotid arteries. These arteries appear to enter the skull at the rostral angle of the posterior lacerated foramen.

Cerebral hemispheres. (Right, figs. 2 and 28.) On the right lateral aspect of the cast the full extent of the exposed course of the rhinal fissure is clearly indicated and the relatively large size of the pyriform lobe at once becomes evident. Above the protuberance of the olfactory tubercle and on the lateral surface of the pyriform lobe two irregular ridges are present corresponding

to skull grooves for the lodgement of the middle cerebral arteries. On the caudo-lateral surface of the pyriform lobe a large obliquely placed ridge indicates the site of a venous sinus (here termed the infero-lateral sinus) which drains backward into the posterior lacerated foramen and communicates with the parieto-temporal channel.

Above the anterior rhinal fissure a small triangular depressed area is present which was termed the trigonum Sylvii in my preliminary report (l. c.). At that time the significance of the unusually rostral situation of this area was not clearly understood. However, subsequent examination of the corresponding region in the other casts, especially in Specimen V, leaves but little room for doubt as to the true homologies of the parts in question (vide infra).

The trigonum Sylvii is bounded in front by the presylvian sulcus which rostrally is bent sharply downwards towards the anterior rhinal fissure. This is due to the overlapping of the presylvian area by the prominent rostro-lateral gyri, in front of which the presylvian sulcus may again be identified.

Dorso-caudally the trigonum is limited by two opercular masses bounded respectively by the anterior and posterior ectosylvian sulci. At the junction of these sulci a small but distinct depression is evident. Above this depression and separated therefrom by but a slight interval is a small oblique sulcus which has been identified as the processus acuminis ectosylvii.

The suprasylvian sulcus is well marked and at its caudal end shows a slight bifurcation. Rostrally the suprasylvian sulcus does not appear to be joined to the corono-ansate sulcus, in which relation it differs from the condition obtaining at the left side of this cast and on both hemispheres of all the other specimens examined. A slight downwardly directed notch is evident on the course of this sulcus at a level somewhat rostrad of the processus acuminis ectosylvii. A short distance caudad of the latter sulcus and parallel to it, a sulcus is present which from its relations has been termed the ramus descendens suprasylvii.

The lateral sulcus forms a deep and well marked groove on the dorsal aspect of the hemisphere. It is not connected with the corono-ansate sulcus.

In the middorsal line the elevation corresponding to the superior sagittal sinus is prominent. This ridge increases in size from before backward and is lost in the tentorial groove on the right side. There is, however, an indication of a small channel draining to the left on this specimen (v. fig. 3).

(Left, figs. 1 and 27.) The conditions on the left side of this specimen closely approximate those on the right except for the juncture of the suprasylvian and corono-ansate sulci as already noted.

On both sides of this specimen the gyri surrounding the rostral extremity of the coronal sulcus are very prominent. Between these two prominent bosses a well marked quadrangular depressed area occurs on the dorsorostral surface of the cast. The most prominent gyri on the cerebral surface other than the coronal bosses are those on each side of the cast which lie between the suprasylvian and the caudal halves of the lateral sulci.

Specimen II (figs. 5 to 10 and 31 to 36).

In the preparation of this specimen, throughout its whole dorsal endocranial surface the fossilized skull bones showed a strong tendency to adhere to the softer underlying natural cast. For this reason a record was kept of the course of the cerebral fissures, etc., during the progress of enucleation of the cast while in the cerebellar portion it was found more practical to clean the endocranial surface of the skull fragments and make a plaster cast of the reassembled parts.

The greatest transverse diameter of the cerebral portion of the natural cast is 4.5 cm. while the maximum interpyriform diameter is 4.5 cm. The maximum fronto-occipital diameter of the cerebrum is 4.4 cm. and its maximum height is 3.3 cm. The maximum transverse diameter of the cerebellar portion of the cast is 3.3 cm. and the maximum height from the basi-occipital or pontine surface to the dorsum of the cerebellum is also 3.3 cm. The volume of the cerebral portion of the cast is 33 cc., that of the cerebellum and brain stem being 13 cc.

Brain stem and basis cerebri. (Fig. 8.) The general plan of the structures in relation to the basis cerebri in this specimen is

the same as in Specimen I. The ridges corresponding to the internal carotid arteries are, however, larger and much more clearly marked. Two thread-like and somewhat tortuous vascular ridges are also evident on this cast, each beginning at the posterior lacerated foramen in close association with the internal carotid ridge and ramifying between this vessel and the midline in the area immediately rostral of the depression for the posterior clinoid processes. These ridges evidently correspond to small arterial vessels and may represent the posterior communicating arteries, though in modern ruminants and suidae the vessels bearing this name are most variable in their development and are commonly not lodged in bony grooves.

The shape of the pituitary protuberance also presents an interesting variation in so far as in its rostral portion it is much broader and more deep and shows evidence of bilateral symmetry, having an ill defined median ridge over its most prominent part. Between the pituitary prominence and the base of the chiasma ridge is a well marked and somewhat bulging area which from its surface configuration apparently marks the site of the infundibulum. The caudal portion of the pituitary prominence is depressed and the fossa occupied by the posterior clinoid processes is somewhat deeper than in Specimen I.

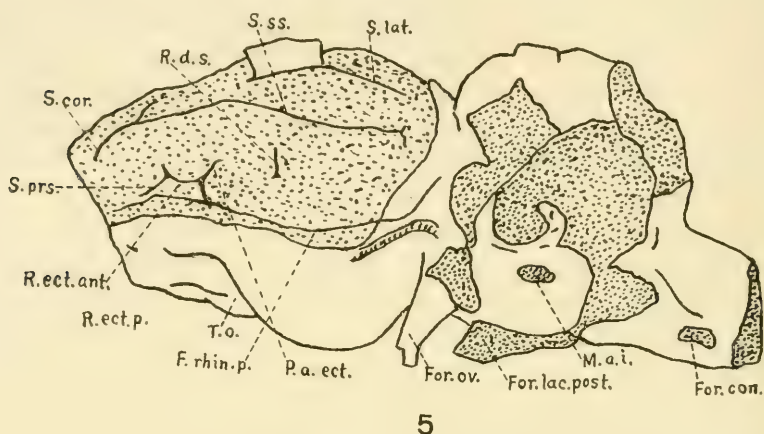
The broad caudal expansions of the pyriform lobes are each marked by shallow longitudinal grooves.

Immediately caudad of the posterior clinoid depression a slight bulging of the smooth basioccipital surface apparently indicates the site of the pons. This bulge is limited caudally by an indistinct transverse groove in which are two minute but distinct depressions. Laterally this region is bounded by ridges corresponding to the posterior lacerated foramen. The two eminences corresponding to the precondylar foramina are evident on the lateral aspects of the caudal part of the myelencephalic base.

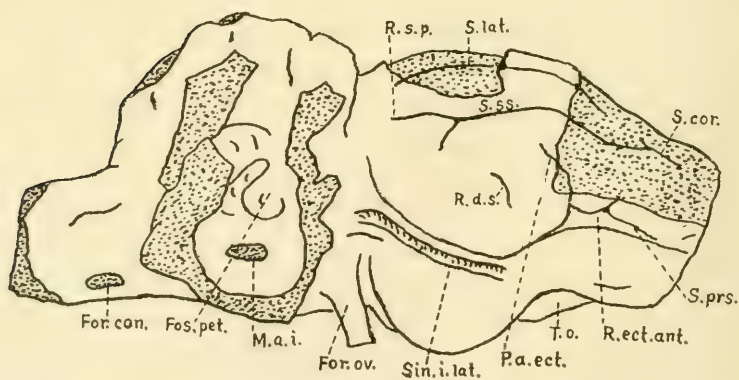
The lateral surfaces of the brain stem are moulded in a characteristic fashion by the petrotic bones. These structures are indicated by smooth depressed areas bounded on their lower margins by the posterior lacerated foramen and each marked in its

center by a prominence corresponding to the meatus auditorius internus.

Cerebral hemispheres. But little requires to be said in the description of this portion of the cast save to note that the convolutional pattern on both right and left sides is practically iden-



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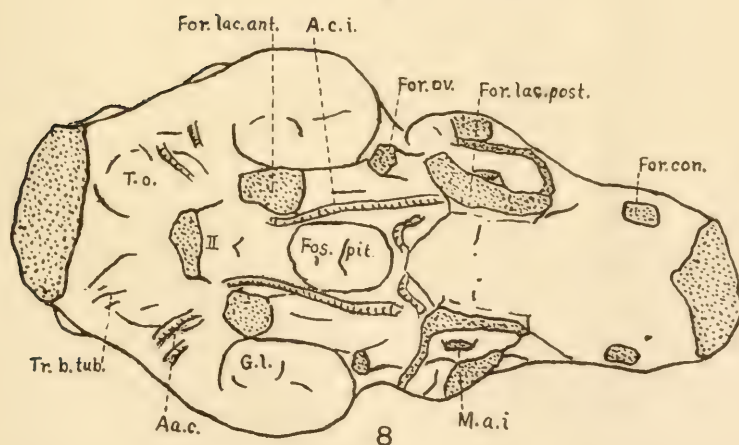
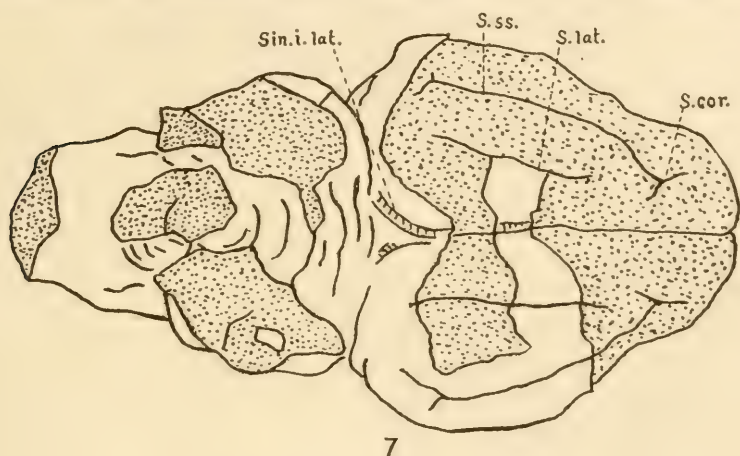


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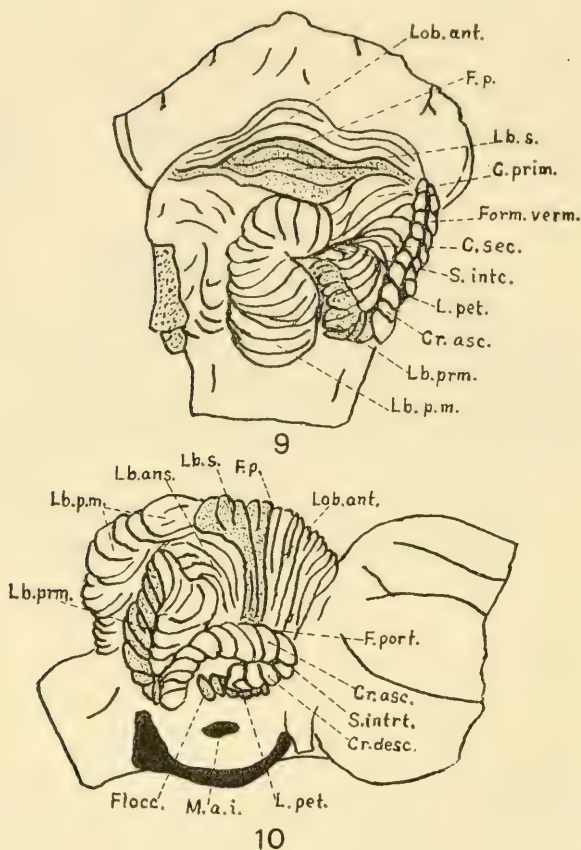
Figs. 5, 6, 7 and 8 Camera lucida drawings of natural endocranial cast of *Oreodon*, Specimen II, left lateral, right lateral, dorsal and ventral views respectively. For photographs see figures 31 to 34. Abbreviations: *For. cond.*, broken surface corresponding to precondylar foramen; *For. lac. post.*, broken surface corresponding to posterior lacerated foramen; *M. a. i.*, broken surface corresponding to internal auditory meatus. Other abbreviations as before.

tical with that obtaining on the left hemisphere of Specimen I. In Specimen II, however, the processus acuminis ectosylvii is evident in its entirety.

As in specimen first described the olfactory lobes are wholly missing from Specimen II. The ridges for the infero-lateral



venous sinuses are evident on the caudo-lateral surfaces of the pyriform lobes in the same relation as in Specimen I, but the superior sagittal sinus differs from that of the latter in deviating in its entirety towards the left side.



Figs. 9 and 10 Camera lucida drawings of plaster endocranial cast of cerebellar fossa of *Oreodon*, Specimen II, dorsal and right lateral views respectively, partially restored. For photographs see figures 35 and 36. Abbreviations: *C. prim.*, crus primum of ansiform lobule; *C. sec.*, crus secundum of ansiform lobule; *Cr. asc.*, ascending crus of pars tonsillaris of formatio vermicularis; *Cr. desc.*, descending crus of pars tonsillaris; *F. p.*, fissura prima; *F. paraf.*, fissura parafoveolaris; *Flocc.*, flocculus; *Form. verm.*, formatio vermicularis; *L. pet.*, petrosal lobule; *Lb. ans.*, ansiform lobule; *Lb. prm.*, paramedian lobule; *Lb. p. m.*, posteromedian lobule; *Lb. s.*, lobulus simplex; *Lob. ant.*, anterior lobe; *S. interc.*, sulcus intercruralis of ansiform lobule; *S. intrt.*, sulcus intratonsillaris. Other abbreviations as before. The flocculus, lobulus simplex and lobulus paramedianus have been further indicated by shading.

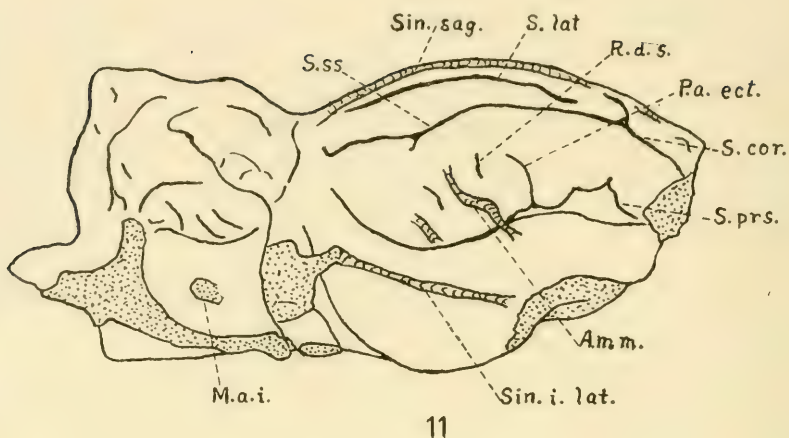
Cerebellum. (Figs. 9, 10, 35 and 36.) The details of the external configuration of the cerebellum are reproduced with remarkable clearness on the endocranial surface of the skull of this specimen. Figures 35 and 36 are photographs of the plaster cast of this region, while figures 9 and 10 are camera lucida drawings of the cast in which all the essential details of the cerebellar morphology have been restored on the right side. The only difference between the details of the photographs and those of the drawings lies in the deletion on the latter of the irregularities caused by the temporo-parietal canal and its associated venous channels and the restoration of the underlying parts.

Reference to figures 8 and 9 renders detailed description of this cast superfluous. It should, however, be noted that the lobulus paramedianus⁵ which appears to be somewhat prominent, on the drawings, is in reality placed at the bottom of a depressed area, between the posteromedian and ansiform lobules. The latter lobule is quite well developed and a sulcus intercuralis may be identified. Of the formatio vermicularis, the flocculus is small and almost wholly hidden beneath the projecting folia of the crus descendens of the pars tonsillaris. A small nonpedunculated projecting process of the crus descendens occupies the well marked subarcuate fossa excavated beneath the prominence corresponding to the superior semicircular canal. This appendage constitutes therefore the homologue of the lobulus petrosus of carnivores.

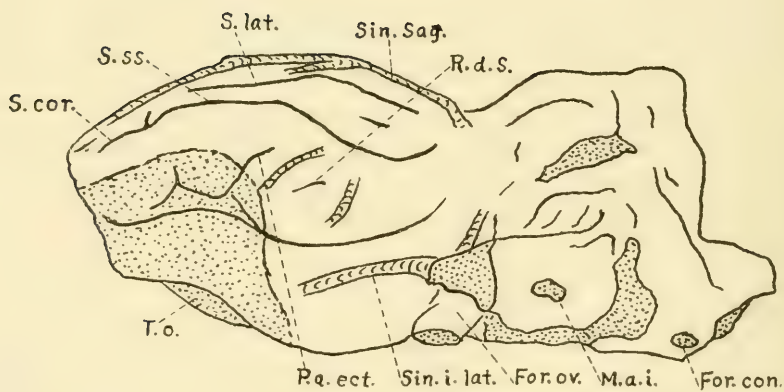
Specimen III (figures 11 to 14 and 37 to 40).

In this specimen a considerable part of the ventral cerebral surface of the cast had been exposed to weathering action and the olfactory bulbs together with a small piece of the rostral part of the cerebrum had been lost prior to being picked up in the field. The extent of the weathered area is indicated in the figures.

⁵ Throughout this paper the nomenclature used in the description of cerebellar parts is that of Bolk (4). The importance of the general adoption of this nomenclature has elsewhere been emphasized (2).

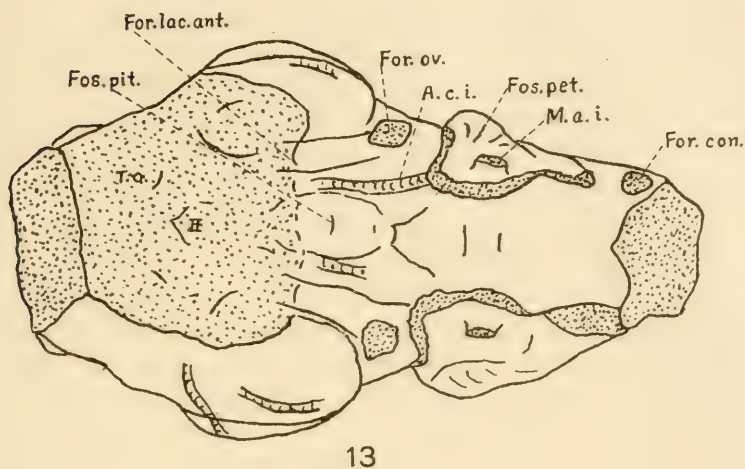


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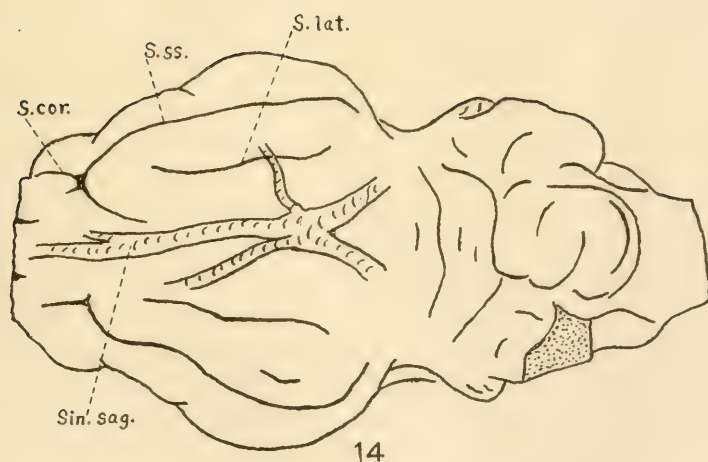


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Figs. 11, 12, 13 and 14 Camera lucida drawings of natural endocranial cast of *Oreodon*, Specimen III, right lateral, left lateral, ventral and dorsal views respectively. For photographs see figures 37 to 40. Abbreviations: *A.m.m.*, ridges corresponding to branches of the middle meningeal artery; *Fos.pet.*, eminence corresponding to subarcuate fossa of the petrous bone. Other abbreviations as before.



13



14

The maximum diameter of the cerebral portion of the cast is transverse and measures 4.6 cm. The maximum interpyriform diameter is 4.4 cm. The maximum fronto-occipital diameter is 4.4 cm. and the maximum height is 3.3 cm. In the cerebellar portion of the cast the greatest transverse diameter is 3.5 cm. and the greatest ponto-dorsal height is 3.4 cm. The volume of

the cerebral portion of the cast is 35 cc., that of the cerebellum and brain stem being 13 cc.

Brain stem and basis cranii. (Fig. 13.) The ridge corresponding to the internal carotid artery is indistinct on the right side of this cast in the neighborhood of the foramen lacerum posterior, though its fellow on the left presents relations similar to those obtaining in Specimen II. No indication can be made out of a transverse connection between these arterial ridges.

The depression for the lodgement of the posterior clinoid processes is somewhat deeper than in Specimens I and II. An ill defined transverse retro-pontal depression may be distinguished and a short distance caudal to it a second similar depression occurs. The latter is placed on a level with the caudal margins of the internal auditory meati and possibly corresponds to the inferior margin of the trapezoid body. The foregoing slight irregularities on the basi-occipital surface of this specimen may be felt distinctly with the finger tips, though they can only be seen in oblique illumination.

The site of the left precondylar foramen is well defined, but on the right side the corresponding area is broken away.

Cerebral hemispheres. In a dorsal view of the cast the ridge corresponding to the skull groove for the superior sagittal sinus is well marked throughout its length. Caudally this ridge bifurcates to the right and left, the former being slightly the larger, and is lost in the wide tentorial groove. Before bifurcation the sagittal ridge is joined obliquely on the left side and almost at right angles on the right side by smaller tributary ridges.

The cerebral fissural pattern on both hemispheres corresponds in all essentials to that obtaining on the left in Specimen I. On the right side of Specimen III there is, however, an additional small compensatory sulcus caudal to the ramus descendens suprasylvii. Further, on the left side of this specimen, expansion of the prominent gyrus lying between the suprasylvian and lateral sulci, has been accompanied by a slight secondary longitudinal folding with the formation of a short secondary sulcus. On the caudo-lateral surface of the pyriform lobes on both sides, the ridge corresponding to the infero-lateral venous sinus is well marked.

Cerebellum. Compared with Specimen II the tentorial groove in the specimen is shallow and indistinct so that the detail of the major part of the lobus anterior is obscured. In addition, the endocranial surface of the skull over the dorsal aspect of this region is marked by numerous irregular vascular channels and minute foramina connecting these channels with diploid spaces. The skull is without doubt that of a young animal, as complete adaptation of the bony parts to the underlying cerebellum has not yet been brought about. Notwithstanding this, the postero-medial lobule has attained to large size and developed the characteristic S-shape of the corresponding lobule in Specimen II. Judging from the manner of growth of the postero-medial lobule in modern forms, it is probable that in *Oreodon* also the lobule in question did not acquire its typical S-shape before the individual had reached adult dimensions. It is therefore probable that the skull is that of a young but full grown animal.

The detail of the arrangement of the formatio vermicularis in this specimen is excellent, particularly that of the crus descendens and its small but well marked lobulus petrosus.

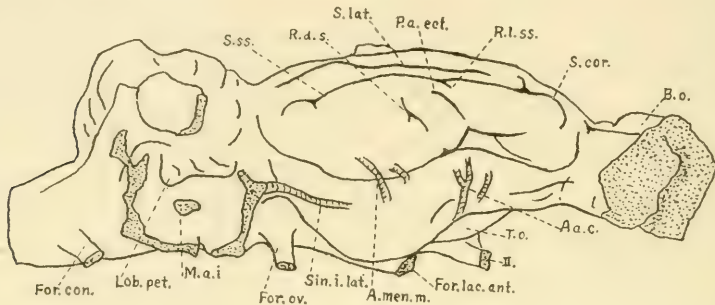
Specimen IV (figures 15 to 18 and 41 to 44)

The entire endocranial cast is represented in this specimen. The greatest transverse diameter of the cerebral portion is 4.6 cm. The maximum interpyriform diameter is 4.5 cm. The maximum fronto-occipital diameter of the cerebrum is 4.6 cm. and its maximum height 3.1 cm. In the cerebellar region the greatest transverse diameter is 3.5 cm. and the ponto-dorsal maximum height is 3.3 cm. The volume of the cerebral portion of the cast is 37 cc., that of the cerebellum and brain stem being 15 cc.

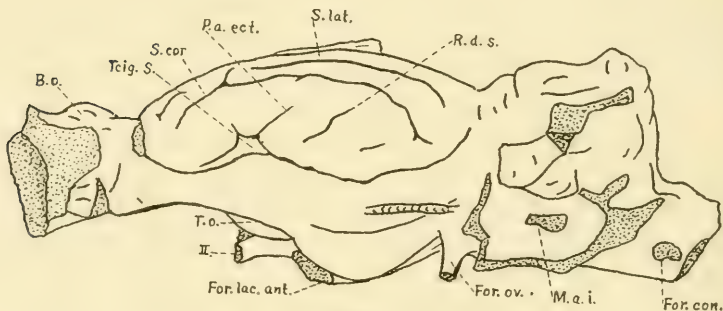
Brain stem and basis cranii. (Fig. 17.) The relations of the ventral surface of the olfactory tract to the tuberculum prominence are well shown in this cast, and particularly so on the right side. Here again may be seen some strand-like markings resembling those already noticed in Specimen I, though not so strongly developed. They are not to be confused with vascular

ridges (several of which mark the caudo-lateral area of the tuberculum) and they are believed to correspond to skull grooves for the lodgement of strands of the tractus bulbo-tuberculare.

The optic foramina as evidenced by the cast are approached by way of an elongated channel somewhat depressed and dumb-



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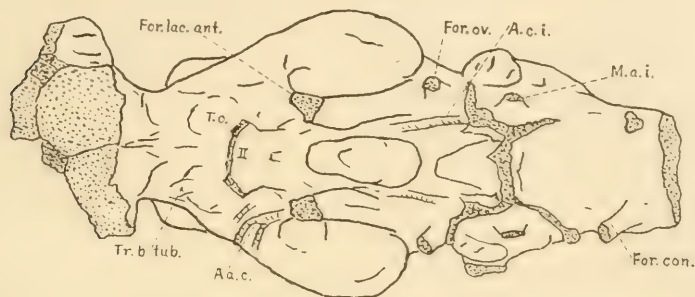


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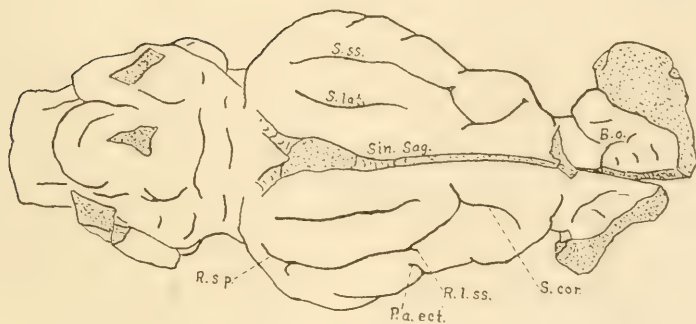
Figs. 15, 16, 17 and 18 Camera lucida drawings of natural endocranial cast of *Oreodon*, Specimen IV, right lateral, left lateral, ventral and dorsal views respectively. For photographs see figures 41 to 44. Abbreviations: *A.men.med.*, ridges corresponding to branches of the middle meningeal artery; *B.o.*, bulbus olfactorius; *R.l.ss.*, ramus lateralis suprasylvii; *R.s.p.*, ramus posterior suprasylvii. Other abbreviations as before.

bell-shaped in cross section. This channel which lodged both optic nerves begins above the shallow pituitary fossa by a single rather wide median aperture and terminates rostrally by bifurcation. These parts thus present in a somewhat more pronounced manner the condition which obtains in this region in *Sus* and *Ovis*.

The fossa for the lodgement of the posterior clinoid processes is shallow and the basioccipital surface between the posterior lacerated foramina is considerably narrower than in the specimens described above. The ridges corresponding to the internal carotid arteries are not so well marked as in Specimen II.



17



18

Cerebral hemispheres. The convolutional pattern of the cerebrum on both sides corresponds quite closely to that obtaining in Specimen III. However, an additional compensatory sulcus behind the ramus descendens suprasylvii is present on the left side in Specimen IV instead of on the right as in the preceding specimen. On both sides a small notch is present on the suprasylvian sulcus just rostrad of the level of the processus acuminis ectosylvii as in Specimen I.

The olfactory bulbs are large, pedunculated and project a considerable distance rostrad of the hemispheres. On their dorsal surfaces they show peculiar and characteristic markings again recalling the condition obtaining in *Orycteropus* (vide supra).

Moodie (l. c., p. 135) states that there are no sacculations to be observed in the frontal sinuses of *Merycochoerus*, an oreodont of Miocene and lower Pliocene age. This author has, however, noted the possibility of a greater development of the frontal sinuses and presence of sacculations in other and more ancient oreodonts. Certainly the peculiar markings upon the dorsal surface of the olfactory bulbs in Specimen IV would suggest the presence of olfactory terminations in the dorsally placed frontal sinuses of *Merycoidodon* such as obtain in certain modern macrostomatic carnivores and edentates.

Cerebellum. The essential details of cerebellar structure are preserved to a large extent on this portion of the cast. This cast is apparently from an animal not completely mature in its development as evidenced by the large vacuities of the parieto-temporal and associated channels as well as by the spongy nature of the endocranial surface over the upper part of the lobulus medianus posterior. This evidence is borne out by the fact that many of the cranial sutures are not obliterated and the tentorial groove is shallow and wide. Judging from the measurements this cast is from a young but full grown adult.

Specimen V (figures 19 to 22 and 45 to 48)

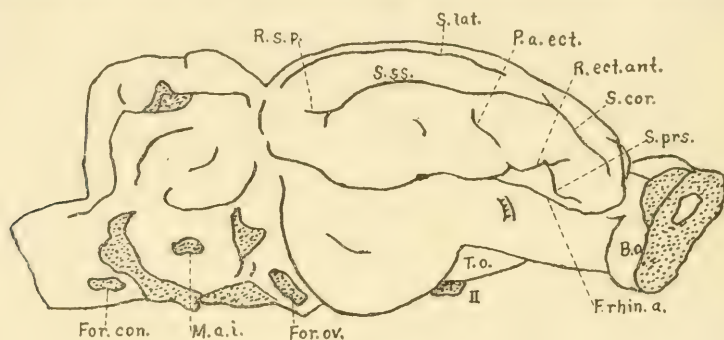
As in the preceding, the entire endocranial cast of this specimen also is preserved. The maximum transverse diameter of the cerebral portion of the cast is 4.7 cm. and its interpyriform maximum is 4.6 cm. The maximum fronto-occipital diameter is 4.5 cm., while the greatest height of the cerebral portion is 3.3 cm. The maximum transverse diameter of the cerebellar portion of the cast is 3.6 cm. and the maximum ponto-dorsal height is 3.2 cm. The volume of the cerebral portion of the cast is 39 cc., while that of the cerebellum and brain stem combined is 15 cc.

Brain stem and basis cranii. (Fig. 22.) The strand-like bulbo-tubercular markings described in the other casts of the series are evident in this specimen also. They are more clear on the left side. The caudal expansions of the pyriform lobes are each marked by longitudinal grooves. Between the prominences of the olfactory tubercles and in front of the chiasma ridge is a small elongated ridge of doubtful significance (vide infra).

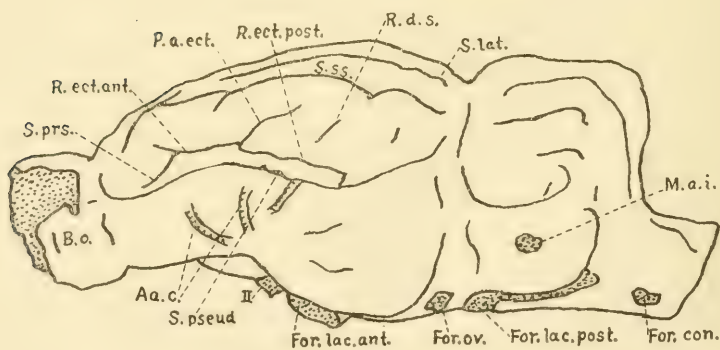
The pituitary eminence is well marked and the ridge corresponding to the left internal carotid artery is equally prominent. The fossa for the lodgement of the posterior clinoid processes is deeper in this specimen than in any other of the series. The basioccipital surface between the posterior lacerated foramina is broader than in Specimen IV and two small pit-like depressions, similar to those observed in the corresponding region in Specimen II, are asymmetrically placed thereon. These depressions are just caudad of the slight transverse pontine ridge. An indistinct transverse irregularity of the basioccipital surface of the cast on a level with the caudal margins of the internal auditory meati may represent the caudal trapezoid boundary.

Cerebral hemispheres. In most essentials the arrangement of the cerebral sulci corresponds with that obtaining in Specimen IV. In one particular, however, the sulcal pattern of this cast presents a most significant variation and differs from that characterizing all the other specimens. The peculiarity in question is more evident on the left side and consists in the presence of an elongated depressed neopallial area contiguous to the rhinal fissure and limited dorsally by a long, slightly arched sulcus. At its caudal end this sulcus cuts the rhinal fissure and rostrally it is continuous with the presylvian sulcus. The cortical area thus circumscribed is overhung above by two opercula bounded respectively by the anterior and posterior ectosylvian sulci. The latter sulci meet to form a well marked processus acuminis ectosylvii. The disposition of limiting sulci about this depressed neopallial area recalls in a striking fashion the condition obtaining in *Hydrochoerus capybara* (Holl, 18, Taf. XVIII, fig. 1; Elliot Smith, 11, fig. 73) and reproduces in all essentials the relations characteristically present in this area in *Moschus* and *Cervus*, and frequently present in *Ovis* and *Capra*.

Cerebellum. On the cerebellar portion of the cast somewhat more of detail has been preserved than in Specimen IV. The tentorial groove is here quite sharply marked and the irregularities of the endocranial surface due to the parieto-occipital and associated venous channels are not very prominent. In all essentials the cerebellar morphology, as evidenced by the surface markings of the cast, corresponds with that of Specimen II described above. In view of these facts as well as on account of



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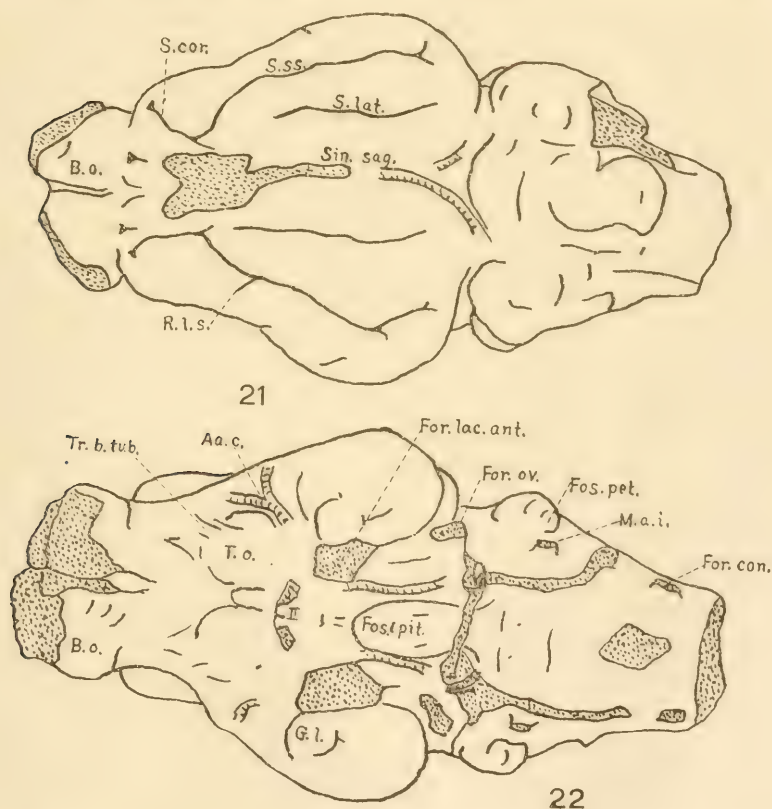
Figs. 19, 20, 21 and 22 Camera lucida drawings of natural endocranial cast of *Oreodon*, Specimen V, right lateral, left lateral, dorsal and ventral views respectively. For photographs see figures 45 to 48. Abbreviations: *Frhin.a.*, anterior rhinal fissure; *S.pseud.*, pseudosylvian notch. Other abbreviations as before.

the measurements of the cast, it is probable that the skull is one of an adult animal somewhat older than Specimen III but not so old as Specimen II.

DISCUSSION

Measurements

Specimen I falls notably below the average both in linear and volumetric measurements, so it is presumed to be from a smaller



animal than the others, possibly an immature specimen. Omitting it from the series, the average measurements of the other four specimens are as follows: maximum transverse cerebral diameter, 4.6 cm.; maximum interpyriform diameter, 4.5 cm.;

maximum fronto-occipital diameter, 4.5 cm.; maximum cerebral height, 3.2 cm.; volume of cerebrum, 36 cc.; volume of cerebellum and brain stem, 14 cc.

The figures given by Flatau and Jacobsohn (15) for *Sus scrofa domestica*, so far as they can be used for comparison, are as follows: Maximum transverse cerebral diameter, circa 4.5 cm.; maximum fronto-occipital diameter, 7.3 cm.; maximum cerebral height, 4.0 cm.; maximum transverse cerebellar diameter, 4.2 cm. *Sus* is made use of in this connection since its size approximates that of *Oreodon*.

A comparison of the figures shows the larger size of the adult pig brain especially evident in the fronto-occipital diameter, while in maximum transverse cerebral diameter *Sus* and *Oreodon* (respectively 4.5 cm.; 4.6 cm.) are practically the same, when it is recalled that the measurement in *Oreodon* is from the endocranial cast.

My own series of formalin hardened pig brains are all from young animals so that linear comparisons with *Oreodon* are not practical. It is of interest to note, however, that the volume of the cerebrum in my specimens ranges from 55 cc. to 60 cc. and this, though it must fall considerably below the volume of the adult cerebrum, is yet far above the average volume of the cerebrum in the *Oreodon* specimens.

Such disparity is not so obvious on comparing the cerebellar-brain stem volumes of *Oreodon* and immature *Sus*, since in the latter the average was but slightly above 14 cc. The difference, however, is somewhat greater than would at first sight appear since among other things the average volume of this region as determined for *Oreodon* is that of the endocranial cavity while in the *Sus* specimens measured it corresponds to brain parts only.

The above comparisons, though admittedly only approximate, are not lacking in significance since they serve to show, 1) that in *Oreodon* the cerebrum had attained a transverse diameter approximately equal to that obtaining in adult modern *Sus*; 2) that a great discrepancy is evident in the fronto-occipital growth of the brain of *Oreodon* as compared with *Sus*; 3) that the volume

of the cerebrum of Oreodon was much less than that of even immature specimens of *Sus*; and 4) that the disparity between the bulk of the cerebellum in Oreodon and in *Sus* is not so evident as that between the cerebral regions in these forms.

Endocranial blood supply

Arteries. The chief arterial blood supply of the cerebrum appears to have been derived from branches of the internal carotid vessels which differ from those of modern ruminants and suillines in their relatively long, uninterrupted intracranial course. They appear to enter the cranium as in the pig by the posterior lacerated foramen and pass rostrad in well marked bony grooves between those for the lodgement of the ophthalmic-maxillary division of the trigeminus and the pituitary fossa. Their course has been described above where it has been noted that at the level of the foramen lacerum anterius the grooves in question converge slightly and may be traced forwards to the base of the chiasma ridge (v. figure 8, p. 283).

In modern ruminants and pigs the internal carotid arteries break up into a rete mirabile beneath the inner layer of dura immediately after their entrance into the cranial cavity. This is also true of the arterial branches arising in common with the ophthalmic artery from the internal maxillary artery in the sheep (vide Owen, 25; Chauveau, 7; Sisson, 30). It is evident therefore that in Oreodon the intracranial course of the internal carotid artery was not interrupted by the formation of a rete mirabile such as characterizes the vessel in modern artiodactyls.

Crossing the caudo-lateral surface of the tuberculum olfactorium and the lateral surface of the pyriform lobe about the level of the trigonum Sylvii there are to be seen on every cast several irregular ridges, whose outlines are not sharply cut, which correspond to vascular grooves upon the endocranial surface of the orbital wing, or the juncture of this and the temporal wing, of the sphenoid. Since in modern ungulates this part of the endocranial surface is usually sculptured more or less distinctly by

the middle cerebral artery, the grooves in question are to be considered as corresponding to analogous vessels in *Oreodon*. They cannot be traced above a level corresponding approximately to the rhinal fissure either in *Oreodon* or in modern forms.

Large and small branches of the middle meningeal artery are evident as sharply defined ridges on the caudo-lateral surface of all the casts. These ridges may be distinguished readily from those corresponding to the middle cerebral artery by the following characters: 1) the middle meningeal arterial ridges are sharply cut and have the appearance of being pasted on the cast; 2) the origin of the larger ridges is always abrupt and presents a broken surface on the cast since in the lower part of their course these arteries are for the most part enclosed in a bony canal; and 3) their topographical relations on the cast are dissimilar. Only the larger vessels of this nature have been indicated on the drawings of the casts. The difference between middle cerebral and middle meningeal arterial ridges is especially clear in Specimen IV (fig. 16).

In one cast (Specimen II) two small arterial grooves caudad of the pituitary fossa may indicate the presence of posterior communicating arteries. In Specimen V attention has been drawn to the curious elongated prominence situated in front of the chiasma ridge and between the olfactory tubercles. It is possible that this corresponds to a groove upon the orbito-sphenoid caused by one of the anterior cerebral arteries, since I have observed a similar groove corresponding to a large anterior cerebral artery in this relation in one specimen of *Canis*.

Veins. The groove for the superior sagittal sinus is well marked on all the casts. Caudally this sinus bifurcates at the confluens. The resulting branches, forming the so-called lateral sinuses, may show considerable inequality in their size and they diverge from one another at an angle much more acute than is the rule in *Sus* and *Ovis*. The lateral sinuses appear to drain chiefly into the parieto-temporal canals. The latter are also connected with large venous channels which ascend from the medulla along the lateral borders of the paramedian lobules of the cerebellum and which apparently represent the ungulate

occipital sinuses. A medium sized sinus ridge situated on the lateral surface of the caudal part of the pyriform lobe has been termed in the foregoing description the infero-lateral sinus. It drains into the posterior lacerated foramen which is also connected in its caudal part with the occipital sinuses.

Endocranial foramina

The cribriform laminae in *Oreodon* are large and occupy the rostral end of each olfactory fossa. No details as to the arrangement of the fenestrae cribrosae have been ascertained on any of the specimens.

The optic foramina open into the endocranial cavity by a single dorso-ventrally depressed canal in a manner somewhat similar to that obtaining in *Ovis*, and due to the presence of a shelf of bone extending backwards from the orbitosphenoid. The canal is somewhat dumbbell-shaped in cross section as the result of moulding of the bone around the optic nerves.

In proportion to the optic foramen, the foramen lacerum anterius is somewhat smaller in *Oreodon* than in *Sus*. In section it is roughly quadrangular with the shortest axis laterally directed. It gives exit to the ophthalmic and maxillary divisions of the trigeminus and probably also the Nerves III, IV and VI as in modern artiodactyls. The two foramina are separated from one another by a distance relatively much greater than obtains in *Ovis* and *Sus*. As in modern artiodactyls, the foramen rotundum is not present as a separate entity. Thus in all these forms the primitive arrangement for the exit of the maxillary trigeminal division by way of the foramen lacerum anterius has been retained (v. Gregory, 16).

The foramen ovale opens downwards and outwards into a short canal which is separated by a stout bony bar from the foramen lacerum posterius. The endocranial aperture of this foramen is somewhat larger than the ensuing bony canal through which passed the mandibular division of the trigeminus. In modern Bovidae the internal carotid artery is also transmitted

through this foramen but as already noted this is not the case in *Oreodon* which in this respect resembles modern pigs.

The parieto-temporal foramen consists of an irregular vacuity above the petrous bone. The canal affords drainage for the lateral sinus and for other venous channels in this region as described above. The condition obtaining in this region in *Oreodon* resembles that in the modern Bovidae but differs from *Sus*, in which the temporal canal is not developed.

The internal auditory meatus is placed below and slightly in front of the well marked subarcuate fossa of the petrous bone. At the bottom of the short wide canal the crista acustica marks off the antero-superior opening of the facial canal from the postero-inferior acoustic area as in modern ungulates.

The posterior lacerated foramen forms a slit-like irregular opening at the side of the basioccipital. In its rostral part it affords passage to the common carotid artery as already noted and is separated from the foramen ovale by a stout bar of bone.

The precondylar foramina are single and open forwards and outwards. In addition to transmitting the hypoglossal nerves these foramina apparently were also traversed by veins.

*Rhinencephalon*⁶

The olfactory bulbs in *Oreodon* are large (figs. 23 and 24) and are set obliquely upon the rostral extremity of the massive olfactory tracts. From the appearance of the casts of the cavities in which the bulbs were lodged, the impression is gained that the lamina cribrosa extended well back over the dorsal surface of the bulbs, which in their shape and relative size closely resemble those of *Orycteropus* (vide Elliot Smith, 8 and 13). The details of the configuration of the ventral and lateral aspects of the bulbus are unknown but it is safe to conclude that the area for attachment of the primary olfactory fibers extended widely over these surfaces.

As in *Orycteropus*, the large olfactory peduncles are visible in a dorsal view of the brain. Ventrally they give rise to the medial

⁶ The term *Rhinencephalon* is here employed in the sense defined by Elliot Smith (9) in contradistinction to the *Neopallium*.

and lateral olfactory tracts. From the latter, a series of fibers arise which pass obliquely over the rostro-lateral margin of the prominent olfactory tubercles and constitute the tractus bulbo-tuberculare.

Caudal of the tuberculum and between the optic chiasma and the pyriform lobe lies the locus perforatus anticus about which no further details can be given. At the rostro-mesial angle of the ventral surface of the broad caudal expansion of the pyriform lobe, a small circumscribed eminence is present in all the specimens; evidently corresponding to the 'gyrus lunaris' of Retzius which, as Elliot Smith (12) has shown, is really the surface of the nucleus amygdalae. The pyriform lobes are very large in proportion to the size of the neopallium and on either side are sharply demarcated therefrom by the well defined rhinal fissure. In short it may be said that the rhinencephalon in *Oreodon* is developed in a manner characteristic of a highly macrosomatic mammal.

Restoration of brain (figures 23 and 24)

From the data gathered in the study of this series of casts it is possible to arrive at a quite accurate estimate of the general morphology of the brain of *Oreodon*. Since such information to a large extent may be epitomised in the form of drawings, an attempt has been made in this direction in figures 23 and 24. In these restorations the details of brain stem configuration and those of the exposed portion of the midbrain have been added for the sake of completeness and are largely matters of surmise. The details of cerebral and cerebellar morphology, on the other hand, are based on observed facts and must closely approximate the truth.

Neopallium

Sulcus lateralis. In all the specimens examined the lateral sulcus is well marked and shows no tendency towards duplication, branching or other irregularity. The sulcus in question forms a sharply cut groove parallel to the median border of the hemisphere and separated therefrom by a broad slightly depressed

gyrus. Caudally it does not extend below the level of the confluens sinuum and rostrally it reaches to within a short distance of the corono-ansate sulcus, but in no instance joins the latter. In the relations and morphology of its lateral sulcus, *Oreodon* thus conforms to a generalized and primitive ungulate type.

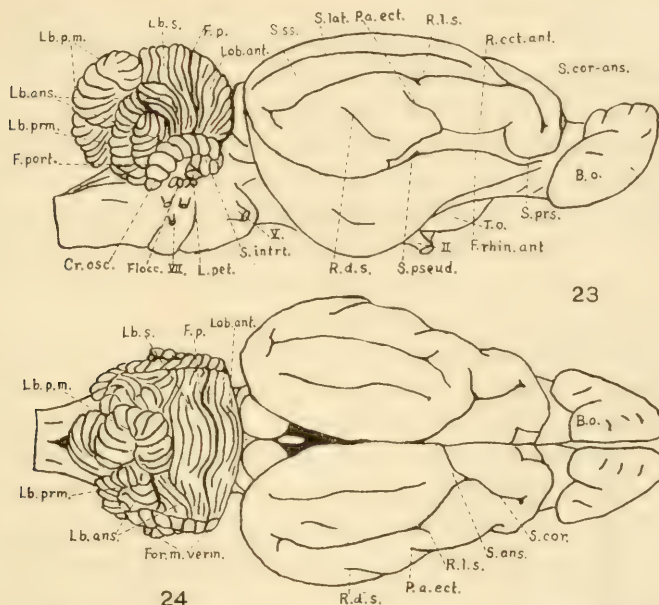
Corono-ansate complex. The coronal sulcus forms a deep, well marked furrow which reaches almost to the frontal pole of the cerebrum and in every specimen the gyrus on its medial side is high and prominent. Caudally the coronal is continuous with an obliquely placed ansate sulcus whose mesial end is closely associated with the margin of the hemisphere and probably cut the latter, as frequently happens among modern artiodactyls (e. g., *Ovis* and *Bos*).

The corono-ansate complex may be independent of the suprasylvian (cf. figs. 3 and 23), but is usually joined to the latter sulcus (in nine of the ten hemispheres examined). The junction of the coronal and suprasylvian sulci in this manner is a condition which characteristically obtains in many modern ruminants. Among suillines, on the other hand, such a condition but rarely occurs and the coronal sulcus is usually joined with the upturned intercalary, a feature which serves to distinguish the members of this group from other artiodactyls. It emerges, therefore, that the relations of the corono-ansate complex in *Oreodon* are of a predominantly ruminant character.

Suprasylvian sulcus. The suprasylvian sulcus extends from the caudal pole of the hemisphere to the level of the ansate sulcus in the form of a wide arch. Its caudal extremity shows a tendency towards bifurcation and the development of a short caudally directed limb. The latter in my preliminary report was spoken of as a possible homologue of the ramus suprasylvii posterior of *Sus*, since though small, its relations are identical with the more constantly developed sulcus bearing this name in modern suillines (cf. Holl, l. c.).

Rostral of the level of the processus acuminis ectosylvii, a small laterally directed notch is frequently present on the suprasylvian sulcus which may correspond to the ramus anterior suprasylvia (Kappers, 19). This sulcus has been termed by Holl the

ramus lateralis suprasylvia (l. c.). It may be present in varying degree in any member of the ungulate group, and evidently depends upon the expansion and consequent folding of the cortex adjacent to the suprasylvian sulcus and dorsal to the anterior ectosylvian operculum. The gyrus situated between the suprasylvian and lateral sulci is especially prominent in all the specimens examined.



Figs. 23 and 24 Restoration of brain of *Oreodon*, right lateral and dorsal views respectively. Abbreviations: *S.cor.ans.*, corono-ansate complex; *II*, optic nerve; *V*, trigeminal nerve; *VII*, facial nerve, above which the two divisions of the auditory nerve are indicated. Other abbreviations as before.

Insular constellation. Ventral to the suprasylvian arch the cortex is folded to form two opercula in a characteristic artiodactyl fashion. The true relations of these parts were only verified after the preparation of the last specimen of the series in which the opercula in question were not fully developed. In all the other specimens the caudal operculum which forms the enlarged caudal lip of the ramus posterior ectosylvii is as highly developed as in *Sus*, and as a consequence the trigonum Sylvii

(Holl) occupies a very rostral position. The rostral opercular fold, over the ramus anterior ectosylvii, is not greatly developed in any of the specimens of the series. The rostral and caudal opercula meet to form a long processus acuminis ectosylvii which almost reaches the suprasylvian sulcus. In the configuration of the ectosylvian complex, *Oreodon* thus reveals certain unique as well as suilline characters.

A notch-like sulcus arises from the rhinal fissure on a plane with the foramen lacerum anterius, which corresponds to the level at which begins the large caudal expansion of the pyriform lobe. This notch, being the result of cortical tension due to the downfolding of the neopallium behind the region of its fixation, probably represents the approximate caudal limit of the underlying corpus striatum as in modern ungulates (v. Holl, l. c.). It is therefore to be considered as the true homologue of the pseudosylvian sulcus of the modern carnivores and ungulates (cf. Holl, also Elliot-Smith, 10).

In the area caudal of the processus acuminis ectosylvii and parallel to it, there is found a sulcus which has been termed the ramus descendens suprasylvii because of its resemblance to the sulcus bearing this name in *Sus*. Holl (l. c.) has considered this sulcus to be the oblique, but as a rule in *Sus* both the sulci mentioned are present as independent furrows. In any case it would seem that the sulcus in question has made its appearance in both *Oreodon* and *Sus* to fulfill similar requirements, viz., to relieve the tension consequent on the sagittal expansion of the caudal ectosylvian operculum.

The rostral boundary of the trigonum Sylvii is marked by a groove which must correspond to the presylvian sulcus of modern ungulates. Apparently it is continuous caudally with the ramus anterior ectosylvii as in *Hydrochoerus* (Holl, l. c.) and as frequently occurs in *Sus*. Frontally it soon becomes hidden beneath the overhanging rostrolateral cortical prominence but it is possible that it may have been prolonged around the frontal pole of the cerebrum to become continuous with a small notch on the mesial surface of the latter. In any case the area of cortex rostral to the presylvian sulcus in *Oreodon* must have been

very small indeed. Thus, while a most primitive arrangement of the part obtains, the presylvian region in *Oreodon* presents certain suilline resemblances.

Cortical projection areas. The general plan of cortical localization has probably been essentially similar in all mammals since the first establishment of neopallial projection centers (v. Elliot Smith, 14). The truth of this conception being granted, the facts as they emerge in the foregoing discussion suggest the following tentative deductions:

1) The visual projection field probably occupied the cortex medial to the lateral sulcus (v. Brodmann, 5).

The gyrus in question is in all cases broad and well developed, and since secondary folding has not been observed it is presumed that it was established early in ontogeny and did not require to alter its original simple configuration in order to attain the requisite area.

2) The auditory projection and association fields probably occupied the lateral neopallium caudal to the processus acuminis ectosylvii, both on the deep and exposed surface of the operculum (v. Campbell, 6).

The area in question is well developed and its chief direction of expansion has evidently been in the sagittal plane, since not only has the posterior operculum been fully developed but its lateral surface has been further increased in area by the development of the ramus descendens suprasylvii. Since both the latter sulcus and the processus acuminis are of simple linear nature, it is presumed that they were not subject to the action of transversely directed cortical stresses during their development and before they became established in much their present form. It is presumed, therefore, that this area was laid down comparatively early in ontogeny (at or about the same time as the visual field) and before the expansion of the prominent gyrus along its medial boundary. The latter gyrus is to be considered as an association field developed later in ontogeny and owing its prominence to its inability to expand laterally.

The topography of such fields as those mentioned above was no doubt the chief factor underlying the great lateral expansion

of the neopallium in *Oreodon*, the transverse diameter of whose cerebrum practically equalled that of *Sus*.

3) The general somatic sensory projection area possibly lay lateral to the corono-ansate sulcus and extended caudally as far as the processus acuminis ectosylvii (v. Campbell, l. c.).

4) The motor projection area probably occupied the cortex medial and to a small extent lateral to the corono-ansate sulcus and extended rostrad to the presylvian sulcus (v. Simpson and King, 29; Campbell, l. c.; Brodmann, l. c.).

Association fields in connection with these last two projection areas would seem to have been but slightly developed, as evidenced by the relatively very small dimensions of the rostral portion of the casts. The prominence of the two gyri bordering the coronal sulcus implies, however, a considerable local functional activity such as might be expected in the somatic sensory-motor projection area of an animal equipped with such a highly organized cerebellum (vide infra).

Cerebellum

The dorsal surface of the cerebellum in *Oreodon* was fully exposed and even a small area of the midbrain must have been visible from above, owing to the slight caudal development of the occipital portion of the neopallium. Among modern forms the nearest approach to such a primitive cerebral condition is to be seen among the Edentates, though in all of the latter forms the occipital neopallial expansion is more extensive than in *Oreodon*. In contrast to this primitive condition of neopallial development, the cerebellum in *Oreodon*, in the arrangement and development of its parts, shows a plan of organization very similar and in no way inferior to that obtaining in modern artiodactyls, while its bulk compares quite favorably with the volume of this organ in *Sus* (vide supra, p. 296).

Lobus anterior and lobulus simplex. Although but little doubt can remain as to the homology with the fissura prima of the well marked transverse depression visible on the dorsum of these casts (vide figures 9 and 10), the anterior lobe and lobulus simplex will be considered together since it is the combined fea-

tures of these parts that reveal their essentially ruminant characteristics.

The area in question is clearly marked out on all the casts as that part of the cerebellum which lies directly rostrad of the prominent postero-median lobule and whose division into medial and lateral moieties is not sharply indicated by grooves. The folia in the mid-dorsal region of this area have expanded to form a characteristic elongated median prominence which merges gradually into the depressed, laterally situated portions. In other words, the chief growth expansion of the folia in this region has been in the sagittal direction and has been greatest in the mid-sagittal plane (v. Bolk, l. c.). As a consequence, the rostro-caudal extent of the area in question when measured in the mid-sagittal plane is practically equal to that of the caudally situated cerebellar parts.

Laterally the depressed portions of this region are encroached upon by the forward growth of the ansiform lobules and so become much reduced in rostro-caudal extent. In spite of this, the part in question is in contact laterally with the crus ascendens of the formatio vermicularis for a considerable distance, being separated therefrom by the rostral part of the fissura parafloccularis.

In all the above features the cerebellum of *Oreodon* shows marked resemblance to that of ruminants (e. g., *Ovis*, *Bos*, *Cervus*) and presents an equally marked contrast to that of *Sus*.

Lobulus medianus posterior. In *Oreodon* this division of the posterior lobe is strongly developed and is folded upon itself to form a sigmoid-shaped lobule which protrudes high above the level of the adjacent anso-paramedian area. A similar development of this lobule is characteristic of most modern ungulates, the few exceptions being chiefly among the smaller members of the group (e. g., *Hydropotes*).

Lobulus ansiformis. This lobule is relatively well developed in *Oreodon* and its folia are apparently arranged in the form of two crura, separated by a short intercrural sulcus. Among modern ungulates a loop-like ansiform lobule is characteristically developed in *Sus* in which the lobule is essential similar to the corresponding region in carnivores. In *Bos* and *Equus* a some-

what similar condition obtains, though in these animals the loop-formation is much less extensive. In other ungulates, however, the two crura of the ansiform lobule and the intercrural sulcus can rarely be distinguished.

Bolk (l. c.) has pointed out that the ansiform lobule constitutes an unpaired center for the elaboration of tonic, sthenic and static impulses for the musculature of the homolateral limbs and in consequence is most highly developed in those forms in which the power of independent limb action has been most perfectly acquired. For this reason the lobule in question is more typically developed in carnivores than in ungulates.

In the latter group, the functional reduction of the limb elements has progressed to the smallest extent in suillines; and in Sus, where both forearm and leg elements are retained as complete and distinct bones, the ansiform lobule is relatively large and characteristically loop-shaped. Among the ungulates, though exceptions occur as noted above, it is evident that a correlation does exist between the development of this lobule and the functional development of the limbs. On this account it is of interest to recall that in Oreodon the bones of the forearm and leg were complete and separate and further that it is probable that a clavicle was also present (v. Scott, l. c.).

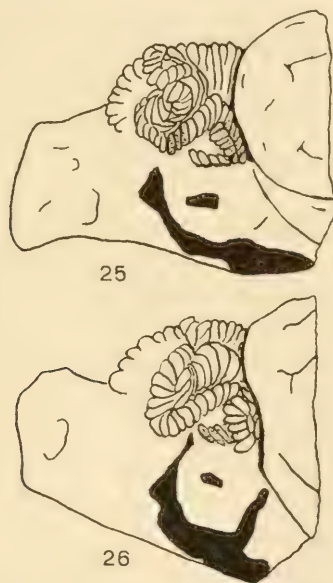
With regard, therefore, to the characters of its ansiform lobule, Oreodon apparently presents resemblances to both suillines and certain ruminants.

Lobulus paramedianus. In Oreodon this subdivision of the posterior cerebellar lobe is overlapped dorsolaterally by the ansiform lobule so that it comes to lie at the bottom of a depressed area between the latter lobule and the lobulus medianus posterior.

Formatio vermicularis. This region of the cerebellum is well developed in Oreodon and is arranged on a plan essentially similar to that obtaining among ruminants (e. g., Ovis, Cervus). At the caudal end of the pars tonsillaris the ascending crus is apparently in continuity with the paramedian lobule while rostrally this crus abuts upon the lateral border of the lobulus simplex and lobus anterior. Here it turns upon itself to become continuous with the crus descendens from which it is separated by

the intratonsillar sulcus. The descending crus is shorter than the ascending limb and terminates at the level of the internal acoustic meatus.

At its caudal termination the folia of the crus descendens form a short non-pedunculated projection which is lodged in the well developed subarcuate fossa of the petrous bone. This projection therefore constitutes a homologue of the lobulus petrosus as



Figs. 25 and 26. Camera lucida outline of the right lateral surface of plaster casts of the cerebellar fossa in *Ovis* and in *Sus* respectively. The relations of the exposed portion of the formatio vermicularis is shown and the parts lodged in excavations of the petrous bone are indicated by shading. For further explanation see text.

defined by Bolk in carnivores, but is not homologous with the cerebellar parts lodged in the so-called 'floccular fossa' of modern ungulates.

The truth of the above assertion becomes evident when the endocranial relations of the cerebellum in this region are examined in *Ovis* and *Sus* (figs. 25 and 26). In *Ovis* the whole terminal bent portion of the crus descendens is lodged in a wide shallow fossa formed between the squamous and petrous portions

of the temporal bone, while caudal of this, and separated therefrom by a bony prominence, a second shallow fossa in the petrous bone lodges a few folia of the caudal part of the crus ascendens. In contrast with this the shallow subarcuate depression in *Sus* lodges a few folia of the flocculus proper. Further, though a slight subarcuate fossa occurs on the petrous bone in *Bos*, *Equus* and *Cervus*, no true petrosal lobule can be distinguished in these forms, a negative character which, as Bolk has already pointed out, they share with all other modern ungulates.

Thus the presence of a true lobulus petrosus in *Oreodon* is a feature apparently unique among modern ungulates, while in other respects the formatio vermicularis is of a generalized ungulate type.

Relation of cerebellum to cerebrum

The large and specialized cerebellum in *Oreodon* is in striking contrast with the small and relatively simply arranged neopallium of this form and affords an excellent example of the apparent independence of these organs during phylogeny.

Palmer's paper on *Anoplotherium* (26) is unfortunately inaccessible to me but Moodie states in his annotation (22, p. 163) that in *Anoplotherium* "the cerebellum is very large and the cerebral convolutions well marked." Since this form was an Eocene mammal it is safe to infer that the neopallium was not very extensive so the disparity between that region and the large cerebellum must also have been marked in *Anoplotherium*.

It would seem, however, that a highly elaborated mechanism for static, sthenic and tonic muscular control, built on lines essentially similar to the corresponding organ of modern mammals could hardly have been evolved independently of the neopallial efferent projection center whose action it supplements. Obviously the alternative suggestion is that the neopallial efferent projection center must have been laid down and functionally active in these early mammals, a conclusion which accords well with the prominent development of the gyri bordering the coronal sulcus (vide supra).

CONCLUSION

As a result of the endocranial data thus accumulated it becomes evident first that *Oreodon* presents certain primitive and generalized characters which may be summarized as follows: A, *primitive characters*: small volume of its cerebrum in comparison with allied modern forms of similar bodily dimensions; limited caudal expansion of the neopallium as evidenced by the exposed dorsum cerebelli; practical absence of presylvian neopallial area; apparently uninterrupted intracranial course of the internal carotid artery (absence of rete mirabile). B, *characters of rhinencephalon*: large terminal olfactory bulbs and extensive lamina cribrosa; massive olfactory tractus and bulbus; macroscopic tractus bulbo-tuberculare; pyriform lobes well developed and very large in proportion to the bulk of the cerebrum above the rhinal fissure. C, *artiodactyl characters*: foramen lacerum anterius transmitting ophthalmic and maxillary division of the trigeminus; foramen ovale for mandibular division of trigeminus; long processus acuminis ectosylvii at junction of rostral and caudal ectosylvian opercula; pseudosylvian sulcus as in modern carnivores and ungulates; lateral sulcus in no case communicating rostrally with corono-ansate; presence of small ramus lateralis suprasylvii of Holl; insular cortex defined by anterior and posterior ectosylvian sulci, rhinal fissure and presylvian sulcus; sigmoid curvature of lobulus medianus posterior of the cerebellum; loop formation of formatio vermicularis cerebelli. In the first analysis therefore it is evident that *Oreodon* was a primitive, macrostomatic artiodactyl.⁷

Oreodon presents, however, other and more determinate endocranial characters which, while confirming its artiodactyl rank, render its status within that order difficult to define. These characters fall naturally into two categories as follows: A, *ruminant characters*: junction of the corono-ansate complex with the

⁷ It is a fact of no small interest that most of the features of the cerebral fissural pattern which are shared in common by modern perissodactyls and artiodactyls and whose presence in some form gives to the brain its so-called 'ungulate' character, are located in the caudo-lateral convex surface of the cerebrum (cf. 'ungulate' ectosylvian, suprasylvian and lateral sulcal configuration).

suprasylvian sulcus in every hemisphere but one examined; relations and extent of lobus anterior and lobulus simplex cerebelli; presence of parieto-temporal canal. B, *suilline characters*: internal carotid artery transmitted through the posterior lacerated foramen; caudal ectosylvian operculum extensive; ramus descendens suprasylvii and ramus suprasylvii posterior as in Sus; course of presylvian sulcus; possible continuity of coronal and splenial sulci in one specimen. Thus the appropriateness of Leidy's original designation of Oreodon as a 'ruminating hog' becomes increasingly evident as the endocranial characters are summarized.

It will be noted that in point of numbers the suilline exceed the ruminant endocranial resemblances in the above list but it remains questionable which should be given the greater weight. On other grounds Osborn and Matthew (v. Osborn, l. c., p. 549) have placed the Oreodontidae under a separate Sectional heading of the Order Artiodactyla, while Gregory (l. c., p. 466) places the family Oreodontidae within his Suborder Ruminantia. A consideration of the possible bearing that the data here collected may have upon the question of the systematic position of Oreodon will be deferred until a study can be made of endocranial casts from contemporaneous Entelodonts and if possible of their Achaenodont precursors.

The endocranial configuration of Oreodon presents no characters that can be considered as specific *per se*. Their specificity depends upon their presence in combination with the generalized and determinate artiodactyl features, and in this sense the following apparently specific characters have been noted: extreme rostral position of the trigonum Sylvii of Holl; presence of a lobulus petrosus cerebelli (as defined above).

To recapitulate, it is evident from a study of its endocranial morphology that Oreodon was a primitive, macrosmatic, artiodactyl ungulate presenting a curious blending of suilline and ruminant characters; and further that any edentate (e. g., Orycteropus) resemblances are of a superficial nature and wholly confined to the rhinencephalon.

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PLATES

PLATE 1

EXPLANATION OF FIGURES

27, 28, 29 and 30 Photographs of the natural endocranial cast of *Oreodon*, Specimen I, left lateral, right lateral, dorsal and ventral views respectively.



PLATE 2

EXPLANATION OF FIGURES

31, 32 and 33 Photographs of the natural endocranial cast of *Oreodon*, Specimen II, right lateral, left lateral and dorsal views respectively.



PLATE 3

EXPLANATION OF FIGURES

34 Photograph of the natural endocranial cast of *Oreodon*, Specimen II, ventral view.

35 and 36 Photographs of plaster endocranial cast of cerebellar fossa of *Oreodon*, Specimen II, dorsal and right lateral views respectively.

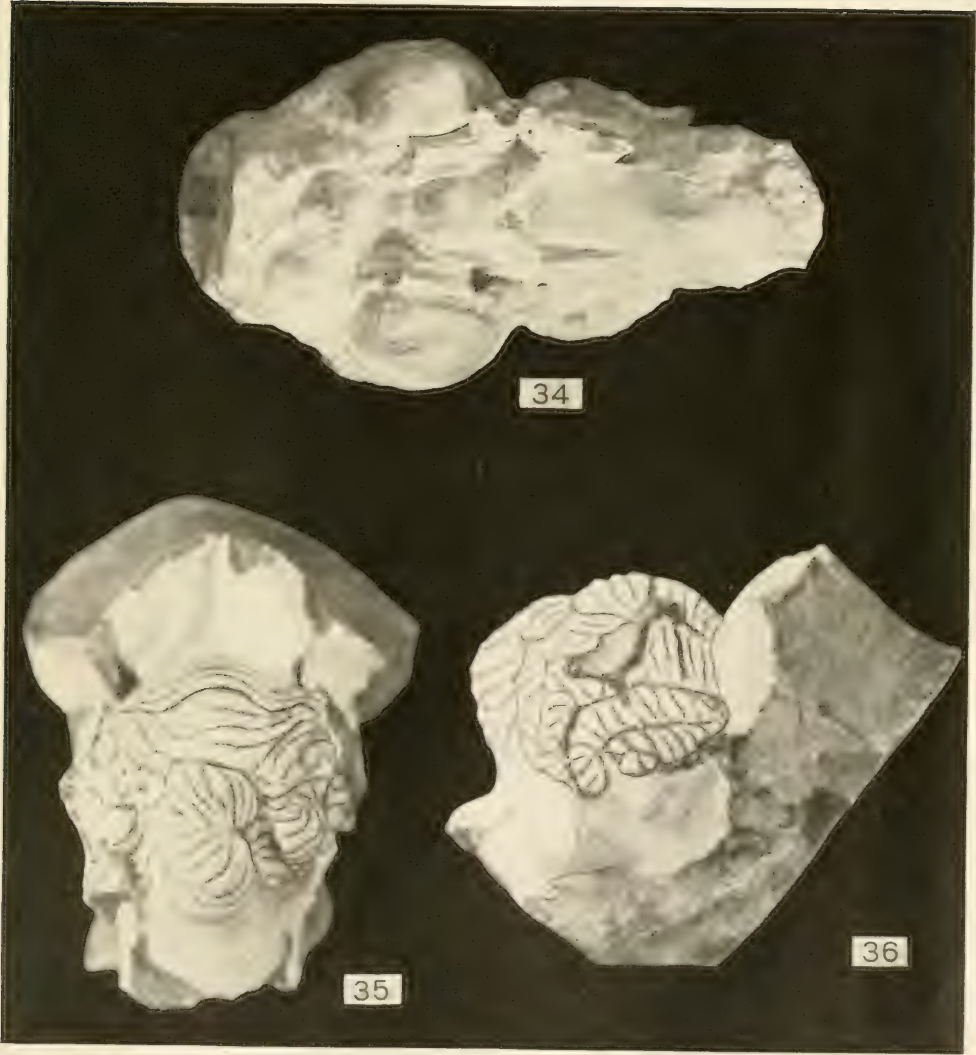


PLATE 4

EXPLANATION OF FIGURES

37, 38, 39 and 40 Photographs of the natural endocranial cast of *Oreodon* Specimen III, right lateral, left lateral, ventral and dorsal views respectively



PLATE 5

EXPLANATION OF FIGURES

41, 42, 43 and 44 Photographs of the natural endocranial cast of *Oreodon*, Specimen IV, right lateral, left lateral, ventral and dorsal views respectively.



PLATE 6

EXPLANATION OF FIGURES

45, 46, 47 and 48 Photographs of the natural endocranial cast of *Oreodon*, Specimen V, right lateral, left lateral, dorsal and ventral views respectively.



Resumen por el autor, Roy Lee Moodie,
University of Illinois.

Exámen microscópico del cerebro de un pez fósil.

El exámen microscópico de secciones de un nódulo que contenía el cerebro de un pequeño pez paleoniscido de las Coal Measures de Kansas ha permitido determinar la existencia de un ancho espacio meníngeo y la posible conservación de las meninges y vasos sanguíneos. El espacio meníngeo está ocupado por calcita vesicular que se separa fácilmente de la superficie del cerebro, nervios y oído. La substancia cerebral está convertida en cristales incompletos de calcita y fosfato.

Puesto que todos los nódulos con cerebros conocidos hasta el presente son casi de la misma naturaleza y substancia, no será posible descubrir vestigios de estructuras neurales microscópicas hasta que se encuentren cerebros fosilizados en un medio diferente. El hecho de que la forma del cerebro no se haya alterado puede explicarse por la naturaleza incompleta de los minúsculos cristales que reemplazaron a su substancia. La formación de estos cristales ha borrado todo vestigio de la estructura orgánica, conservándose tan solo la forma del cerebro. Esta sin embargo se ha conservado con una belleza que no ha sido nunca sobrepasada en material fosilizado.

Translation by José F. Nonidez
Cornell Medical College, New York

MICROSCOPIC EXAMINATION OF A FOSSIL FISH BRAIN

ROY L. MOODIE

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TWO FIGURES

When I published my first study (1) on the ganoid fish brains from the Coal Measures of Kansas I had no material which could be spared for sectioning, although I was extremely anxious to determine if there were microscopic evidences of organic structure in the petrified material. Since that paper appeared I have received through the kindness of my friend, Bennett Mills Allen of Kansas University, a series of nodules containing fish brains which he had collected at the quarry and brought to Chicago for me. Examination of all the specimens under the binocular showed no essential differences in external form of the brain from those previously described, so it was decided to devote one of the brain-containing nodules to sectioning, to find, if possible, traces of fiber paths or nuclei, or any organic structure which might be preserved.

Sections of an entire nodule with its contained brain, which had been slightly chipped to determine the presence of neural structures, were cut for me at the laboratories of the United States Geological Survey by Mr. F. S. Reed, with a thickness of about 12 microns. A favorable region is shown in the photomicrograph (fig. 2) at a magnification of 70 diameters. Owing to the crystalline nature of the material it was not deemed necessary to attempt staining, since an examination of the results of Professor Lignier (2) who stained sections of fossil cycads with vesuvine (Bismark-brown, or tri-amido-azobenzene) and Seitz (3) who used an aqueous solution of Eosin, after a most elaborate technique of preparation of the fossil bones of dinosaurs and

other fossil reptiles, has failed to convince me that there is any advantage in such a complicated method. Sections prepared by the petrographic method, which consists in cutting with a saw and grinding with emery powder on a leaden disc, are fully as

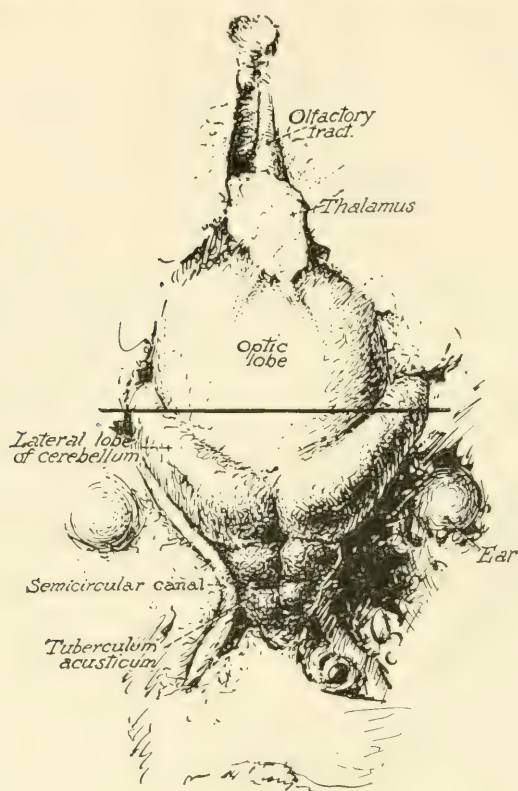


Fig. 1 Brain of *Rhadinichthys deani* Eastman from the Mississippian of Kentucky. $\times 10$. The plane of the section is shown in the heavy transverse line. This brain is almost identical in type with those from Kansas.

useful, and so far as the photomicrographs show fully as capable of exhibiting anatomical detail as the more tedious methods of Lignier and Seitz. This statement is based on an examination of several score of sections of fossil structures, chiefly bone, ranging in age from the Devonian to Recent, all of which have been prepared by the petrographic method. In the present instance

it was well that staining was not attempted, since there are no evidences whatever of organic structure; only the outer form of the brain, nerves and semicircular canals are preserved.

In attempting to solve the problem presented by the preservation of these little fish brains I was at a loss to explain the fate of the meningeal space which in most of the recent fishes is quite

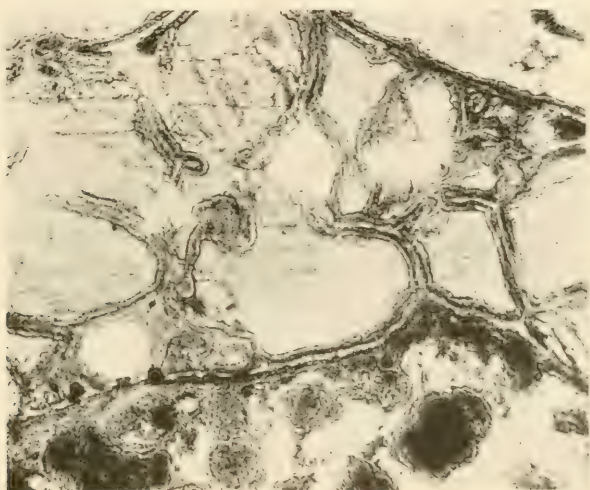


Fig. 2 Photomicrograph of a section through a brain-containing nodule from the Coal Measures of Kansas. $\times 70$. There are three important areas in this untouched photograph: 1) A dark area running entirely across the picture at the bottom, extending about one-third of the distance up the right side, and running obliquely downwards to the left, representing the phosphate or substance of the nodule which has replaced the brain case. The upper surface of this substance then represents the floor of the brain case. 2) A lighter area composed of rounded irregular spaces representing the meningeal space which has been filled with calcite. 3) The substance of the brain itself, or at least a portion of the left cerebellar lobe, showing its structureless nature. This area is seen in the triangular portion cut off by a dark band in the upper right hand corner of the figure. The most important and only new thing established by this figure is the extent of the perineural space, which is seen to be quite large and is comparable to the meningeal spaces of modern fishes.

extensive. The meningeal spaces in the present fish brain are filled with masses of calcite crystals which are separated by threads of calcium phosphate. The phosphatic threads may be the representatives of blood vessels but I doubt it since the same

threads occur in the substance of the nodule itself and the brain substance is entirely free from such threads.

I have shown in figure 2 an enlargement of 70 diameters of a portion of the meningeal space. The dark band at the bottom of the figure is the substance of the nodule, through which the plane of section is indicated in figure 1 by the heavy transverse line cutting the optic lobes and the cerebellar lobes. The light area in the substance of the nodule is calcite, usually entirely crystalline; the dark areas represent the phosphate of calcium and are nearly opaque. On this darker area reposes the meningeal space filled with threads of phosphate and calcite crystals. In the upper right hand corner is a portion of the left cerebellar lobe, which in the photomicrograph appears structureless, but under the microscope and better under the polariscope the substance of the brain is seen to be converted into incomplete crystals of calcium carbonate (calcite) and calcium phosphate. The polariscope shows this substance in a lighter blue than the well-formed calcite crystals in the meningeal space. The transverse striae seen in these latter calcite crystals in the photomicrograph are the orthorhombic cleavage planes of the crystals.

It is suggested elsewhere (4) that the brain substance may have been converted into palmitate or cholesteryl stearate, which enabled it to retain its form until more adequate fossilization could set in. In the present instance, if this were true, it would also explain the preservation of the meningeal spaces which were filled with a calcium magma before true fossilization set in.

There are no traces whatever of either cartilage or bone. The brain case and skull have been completely transformed into calcium phosphate. If the phosphatic portion represents the brain case, and I have every reason to believe it does, then we have the interesting addition to our knowledge of Paleoneurology, and one which justifies the publication of this paper; that is, Carboniferous ganoid fishes of the paleoniscid type had a wide meningeal space as do most modern fishes. This meningeal space is filled with calcite crystals, separated by threads of phosphate giving the substance a vesicular appearance to the naked eye or under low magnification.

SUMMARY

Microscopic examination of sections through a nodule containing the brain of a small paleoniscid fish from the Coal Measures of Kansas has resulted in the determination of a wide meningeal space, and the possible preservation of the meninges and blood vessels. The meningeal space is filled with vesicular calcite which is readily broken away from the surface of the brain, nerves and ear.

The brain substance itself is converted into incomplete crystals of calcite and phosphate. Since all known brain containing nodules are of about the same nature and substance it will not be possible to discover evidences of microscopic neural structures until brains are found fossilized in a different medium. The fact that the form of the brain was not distorted is explained by the incomplete nature of the minute crystals which replaced its substance. The formation of these crystals has obliterated all traces of organic structure, and only the form of the brain is preserved. This, however, is retained in a beauty which has never been surpassed in fossilized material.

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Resumen por los autores, Albert Kuntz y O. V. Batson,
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Observaciones experimentales sobre la histogénesis de los troncos del simpático en el pollo.

Embriones de pollo de cuarenta y ocho horas de incubación fueron sometidos a una operación que consistió en la destrucción de las crestas neurales y porción dorsal del tubo neural en una porción limitada del tronco. Los embriones que sobrevivieron a la operación y continuaron desarrollándose fueron preparados al final del cuarto o quinto día y fijados para estudio.

En algunos de estos embriones faltan los ganglios espinales y las raíces nerviosas dorsales, bien sea en ambos lados del cuerpo o en un solo lado, en una serie de segmentos sucesivos en los cuales existen las raíces ventrales.

Los primordia de los ganglios de los troncos del simpático existen en todos estos segmentos son excepción de unos pocos en los cuales el resto de tubo neural es muy pequeño y las raíces nerviosas ventrales están poco desarrolladas. Indudablemente, estos primordia de los ganglios del simpático se originaron a expensas de células de origen medular que avanzaron periféricamente a lo largo de los caminos seguidos por las raíces ventrales de los nervios espinales.

Translation by José F. Nonidez
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EXPERIMENTAL OBSERVATIONS ON THE HISTO- GENESIS OF THE SYMPATHETIC TRUNKS IN THE CHICK

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THREE FIGURES

INTRODUCTION

According to the older teaching the primordia of the sympathetic trunks arise from cells which become displaced from the spinal ganglia. Some of the more recent investigators who have studied the histogenesis of the sympathetic nervous system have presented evidence which indicates both that cells which become displaced from the spinal ganglia and cells which migrate from the ventral portion of the neural tube take part in the development of the sympathetic trunks; others still maintain that the ganglia of the sympathetic trunks arise exclusively from cells which advance peripherally from the spinal ganglia. The literature bearing on this problem was reviewed recently by one of the present writers (Kuntz '20)¹ and will not be considered further in this paper.

The senior author has for ten years advocated the theory that cells of medullary origin play an important part in the development of the sympathetic nervous system; nevertheless, he has long recognized the limitations of direct observation on normal embryonic material as a method of obtaining conclusive evidence on this point. The cells of ganglionic and medullary origin which become displaced from the cerebrospinal nervous system

¹ The development of the sympathetic nervous system in man. Jour. Comp. Neur., vol. 32, pp. 173-229.

advance peripherally along the paths of the dorsal and ventral roots of the spinal nerves respectively. They are identical in appearance; consequently, in embryos of the higher vertebrates, those from the one source cannot be distinguished from those from the other source after they have advanced beyond the junction of the dorsal and ventral nerve-roots. Therefore, the fact that cells deviate from the paths of the spinal nerves and enter the primordia of the sympathetic trunks does not prove conclusively that these primordia comprise both cells of ganglionic and medullary origin. The chief contentions of those who maintain that only cells which advance peripherally from the spinal ganglia enter the primordia of the sympathetic trunks are: 1) that migration of cells from the ventral part of the neural tube, if it occur at all in embryos of the higher vertebrates, is not abundant, and 2) that such cells as may advance from the neural tube along the fibers of the ventral roots of the spinal nerves become incorporated in the neurilemma.

In view of the present status of this problem it has seemed desirable to obtain crucial experimental evidence regarding the contribution of cells from the neural tube to the primordia of the sympathetic trunks. If the neural crests and the dorsal portion of the neural tube could be eliminated before the spinal ganglia have become differentiated and the embryo could continue to develop without spinal ganglia and dorsal nerve-roots, the remaining portion of the neural tube would be the only source from which cells of nervous origin could migrate along the paths of the spinal nerves. If in such embryos the primordia of the sympathetic trunks should arise, they would of necessity arise from cells which migrate from the neural tube along the paths of the ventral roots of the spinal nerves.

The observations set forth in this paper are based on embryos of the chick which were early subjected to an operative procedure by which the dorsal portion of the cerebrospinal nervous system was destroyed throughout a limited portion of the trunk region. This material affords conclusive evidence that cells of medullary origin which advance peripherally along the ventral roots of the spinal nerves enter the primordia of the sympathetic trunks.

TECHNIQUE

The operative technique employed does not differ essentially from that which was described recently by Clark ('20).² The destruction of tissue was accomplished by electrolysis. The negative electrode, which was placed on the region to be destroyed, consisted of a very fine metallic filament.

The embryos were subjected to operation at the close of the second day (48 hours) of incubation. At this time the spinal ganglia are not yet differentiated, and in the posterior portion of the trunk the neural tube is not yet closed. An attempt was made to destroy just enough tissue along the dorsal aspect of the embryo to insure the complete elimination of the neural crest material, but to leave the ventral half of the neural tube intact. It is quite impossible at the time of operation to determine just how much tissue is destroyed. In some instances the desired result was obtained; in others either the destruction of tissue was not sufficiently extensive to insure the complete elimination of the spinal ganglia, or it was so extensive that the neural tube was almost or completely destroyed. Two of the embryos which survived the operation and continued to develop were killed at the close of the fourth day (96 hours); the others at the close of the fifth day (120 hours) of incubation.

DESCRIPTION OF MATERIAL

A total of seven embryos in which the operation was effective survived until they were killed to be prepared for study. In all of these the portion of the trunk involved showed some distortion, otherwise the embryos were quite normal in appearance. Sections of these embryos indicate a marked degree of regeneration of tissue in the effort to repair the injury caused by the operation. Throughout the greater part of the region involved in all of the embryos the neural canal is closed and the mesodermal and ectodermal layers are completed dorsally. However, wherever the neural crests and the dorsal portion of the neural tube

² Technique of operating on chick embryos. *Science*, N. S., vol. 51, pp. 371-373.

were successfully destroyed these parts are not restored. Most commonly the remnant of the neural tube as repaired contains a single small neural canal which is lined by an endodermal layer. At certain points an attempt at duplication occurred in which two small neural canals were formed. At some points the operative procedure apparently caused some displacement of masses of nervous tissue which continued to live. At such points may be observed the rudiments of three or four distorted neural canals.

In one of the embryos which were killed at the close of the fourth day of incubation development was materially retarded; in the other only the posterior portion of the trunk was involved in the operation. In one of the other embryos the destruction of tissue was not sufficiently extensive to insure the complete absence of spinal ganglia except in a few segments on one side only. These three embryos were discarded for the purposes of this study. The following observations are based on preparations of the four remaining embryos all of which were killed at the close of the fifth day (120 hours) of incubation.

NUMBER 1. In this embryo the operation involved the nervous system throughout the lower thoracic, lumbar and sacral regions. The destruction of tissue occurred asymmetrically. In the thoracic region spinal ganglia and dorsal nerve-roots are absent unilaterally in four successive segments. In the next two segments the spinal ganglia are represented by small aggregates of ganglion cells and the dorsal nerve-roots by relatively few fibers. Continuing caudad spinal ganglia and dorsal nerve-roots are completely absent on the same side in several successive segments. Spinal ganglia and dorsal nerve-roots are present on the opposite side in all of these segments. In some segments they are approximately of normal size; in others they are materially reduced. The primordia of ganglia of the sympathetic trunks are present bilaterally in all of these segments. Obviously, the primordia of the sympathetic ganglia which are associated with those spinal nerves which are represented by the ventral roots only arose from cells which advanced from the neural tube along the paths of these ventral nerve-roots. Farther posteriorly the destruction of nervous tissue was more extensive, and

the sections indicate considerable distortion. In a few segments in this region in which small ventral nerve-roots are present the primordia of the sympathetic trunks are wanting.

The conditions which obtain in one of the thoracic segments on the side on which the spinal ganglion and dorsal nerve-root are absent are illustrated in figure 1. In this segment the ventral nerve-root is relatively large. There is also evidence of abundant migration of cells of medullary origin along its fibers. That such migration was still in progress at the close of the fifth day of incubation is indicated by the fact that continuous lines of cells may be traced from the motor nidulus into the ventral nerve-root and that cells of medullary origin are abundant in the proximal portion of the nerve. Such cells are present also along the fibrous communicating ramus which connects the primordium of the sympathetic trunk with the spinal nerve. This primordium is approximately as large as the primordium of the sympathetic trunk on the opposite side in this segment where both spinal ganglion and dorsal nerve-root are present.

In order to show approximately what portion of the neural tube is wanting in this segment, a camera lucida outline of the entire cross section of its remnant is superimposed (figure 1, A) on a camera lucida outline of the same magnification of a cross section of the neural tube a few segments farther cephalad where it was not affected by the operation.

NUMBER 2. In this embryo the operation involved the nervous system in the lumbar and sacral regions. In the anterior portion of the region involved the neural tube is almost completely absent. In a few segments only a few small masses of nervous tissue remain along the dorsal aspect of the notochord. From these masses fibers which, doubtless, represent the ventral roots of the spinal nerves grow out on one or both sides in each segment. Continuing caudad a larger portion of the central nervous system is left intact. Transverse sections show a small distorted neural tube which contains a small but complete neural canal. In a few segments small groups of nervous elements lie outside the neural tube. These may or may not be cells of neural crest origin. Ventral nerve-roots as well as fibers which emerge

from the cell-masses lying outside the neural tube are present in these segments. In the posterior portion of the region involved in the operation the destruction of tissue was less extensive. In these segments the ventral portion of the neural tube appears nearly normal. The dorsoventral diameter of the neural tube is materially reduced. Two small neural canals each of which is surrounded by an ependymal layer are present. One of these canals occupies the position of the ventral portion of the normal neural canal; the other lies in an asymmetrical position in the dorsal portion of the remnant of the neural tube (fig. 2). In several segments at this level spinal ganglia and dorsal nerve-roots are absent unilaterally. On the opposite side nerve cells lying outside the neural tube but not apparently involved in the ventral nerve-roots are present in all of these segments. These cell-aggregates may be of neural crest origin, but they do not constitute definitive spinal ganglia. Cell-aggregates which constitute the primordia of the ganglia of the sympathetic trunks are present in every segment in which there is a well defined ventral nerve-root throughout the entire region affected by the operation; consequently, the primordia of the sympathetic ganglia in those segments in which the spinal ganglia and dorsal nerve-roots are wanting must have arisen from cells which advanced from the neural tube along the paths of the ventral nerve-roots.

Figure 2 is taken from a section from one of the segments in which the remnant of the neural tube contains two neural canals and from which the spinal ganglia and dorsal nerve-root are absent. In this segment a sympathetic primordium of considerable size is connected with the ventral nerve-root by means of a fibro-cellular communicating ramus. The presence of numerous cells of nervous origin along the spinal nerve and the communicating ramus suggests that migration along this path has not yet ceased. The primordia of the prevertebral plexuses are already present. A few nerve-fibers emerge from the dorsal portion of the remnant of the neural tube in this segment; however, they do not join the ventral nerve-root, but grow into the differentiating myotome. The relation of these fibers to the myotome suggests that they are not sensory, but motor fibers; consequently, they do not represent the dorsal nerve-root.

NUMBER 3. In this embryo the operation involved the nervous system in the lower thoracic and lumbar regions. The neural tube is reduced to less than one third its normal size in not less than ten successive segments. Spinal ganglia and dorsal nerve-

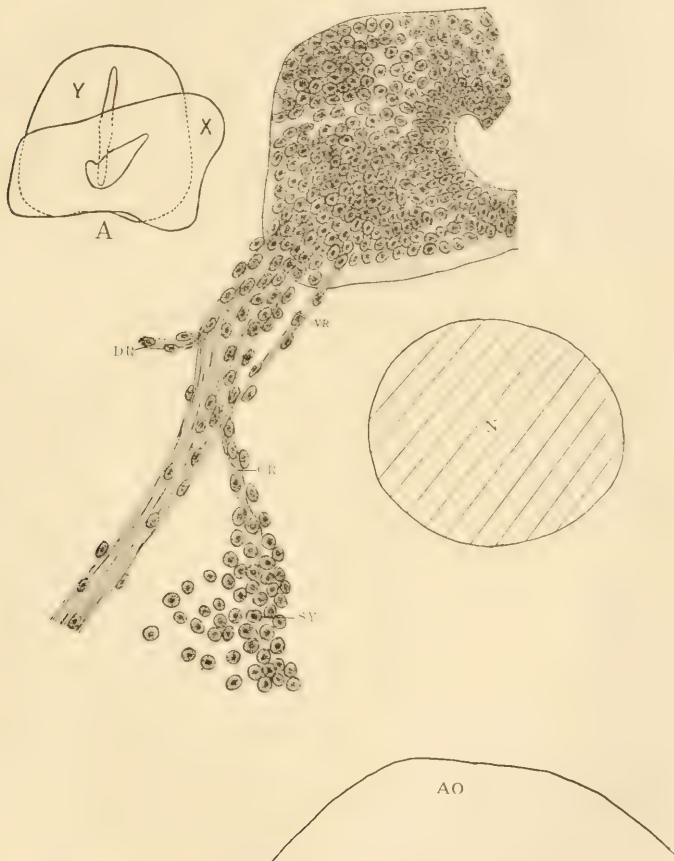


Fig.1 Transverse section from a segment of embryo number 1, in which spinal ganglion and dorsal nerve-root are absent. $\times 165$. AO, aorta; CR, communicating ramus; DR, dorsal ramus; N, notochord; SY, sympathetic trunk; VR, ventral root of spinal nerve.

A. Camera lucida outline of a cross section of the remnant of the neural tube (X) in the segment from which figure 1 is taken superimposed on a camera lucida outline of the same magnification of a cross section of the neural tube (Y) a few segments farther cephalad where it was not affected by the operation.

roots are entirely absent in at least six successive segments. Nevertheless, sympathetic primordia related to the ventral roots of the spinal nerves are present bilaterally in all of these segments.

Figure 3 is reconstructed from several sections from one of the segments in this series. In order to show approximately what portion of the neural tube is wanting at this level, a camera lucida outline of the cross section of its remnant is superimposed (fig. 3, A) on a camera lucida outline of the same magnification of a cross section of the neural tube taken several segments farther cephalad where it was not affected by the operation. As indicated in figure 3, a small aggregate of cells of nervous origin which is not incorporated in the wall of the neural tube lies along one of its dorsolateral aspects in the segment from which this figure was taken. Apparently a few cells migrate from this cell-aggregate along the ventral nerve-root. In view of the extensive destruction of the nervous tissue which occurred at this level it is quite improbable that these are cells of neural crest origin. They probably represent cells of medullary origin which became somewhat displaced by the operative procedure and did not again become incorporated in the wall of the neural tube. No cells similarly located were observed on the opposite side in the same segment nor on either side in any of the other segments in this series. As indicated in the figure, the sympathetic primordia in this instance are relatively small and somewhat asymmetrical.

NUMBER 4. In this embryo the operation involved the nervous system from the level of the anterior to the level of the posterior limb-buds. The destruction of tissue was somewhat more extensive in this case than in any of the others. In several segments in the anterior portion of the region involved the central nervous system is represented by a very slender column of nervous tissue in which there is no neural canal. Advancing caudad the remnant of the neural tube becomes somewhat larger and contains a small neural canal. Farther posteriorly it again becomes smaller until at a level just anterior to the posterior limb-buds the central nervous system is entirely absent. Spinal ganglia and dorsal nerve-roots are absent bilaterally in every

segment from the level of the anterior to the level of the posterior limb-buds. Ventral nerve-roots are present bilaterally or uni-

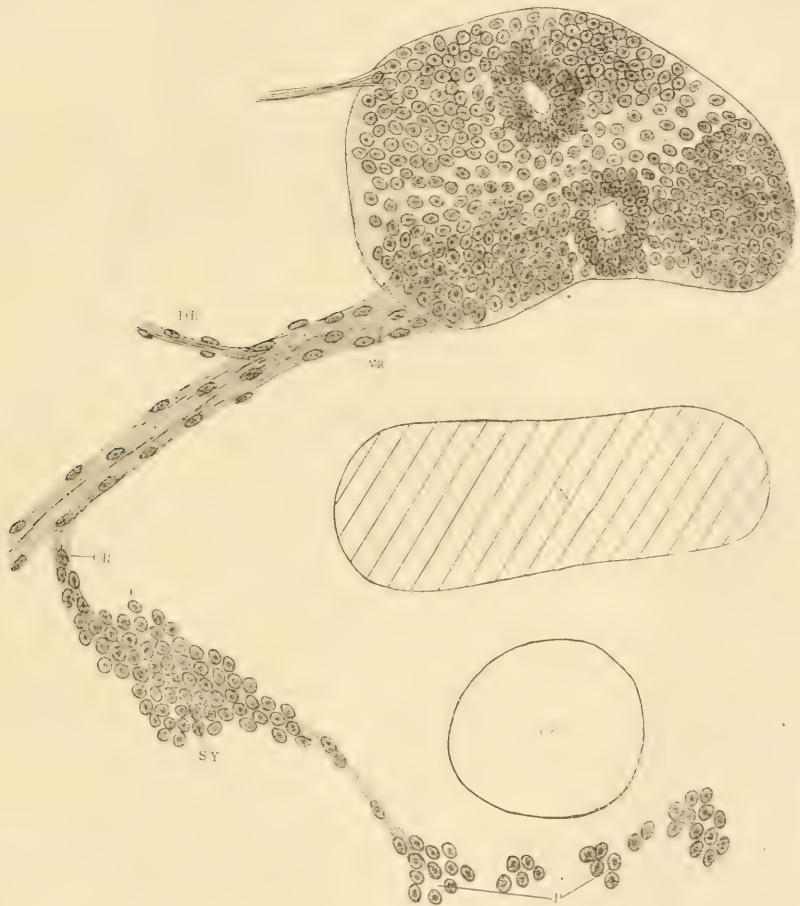


Fig. 2 Transverse section from a segment of embryo number 2, in which two neural canals are present and spinal ganglion and dorsal nerve-root are absent. $\times 165$. AO, aorta; CR, communicating ramus; DR, dorsal ramus; N, notochord; P, prevertebral plexus; SY, sympathetic trunk; VR, ventral root of spinal nerve.

laterally in every segment in which there remains an appreciable remnant of the neural tube. Some of these ventral nerve-roots comprise relatively few fibers; others are larger, but none are of

CONCLUSIONS

The observations recorded in the preceding pages demonstrate clearly that the primordia of the ganglia of the sympathetic trunks may arise in the absence of spinal ganglia and dorsal nerve-roots; consequently, cells of medullary origin which advance peripherally along the paths of the ventral roots of the spinal nerves enter these primordia. The spinal ganglia are not excluded as a source from which cells may enter the primordia of the sympathetic trunks under normal conditions; however, these primordia may arise from cells derived from the neural tube only, at least when cells which have their origin in the spinal ganglia (or neural crest) are excluded.

As observed above, the primordia of the ganglia of the sympathetic trunks may be approximately of normal size in segments in which the spinal ganglia and dorsal nerve-roots are absent, but the remnant of the neural tube is relatively large. On the other hand, these primordia are small or entirely absent in segments in which the remnant of the neural tube is small and represents only the most ventral portion of the central nervous system, even though ventral nerve-roots are present. These facts suggest that the cells which normally give rise to the ganglia of the sympathetic trunks are derived largely from those portions of the walls of the neural tube which give rise to the lateral cell-columns. Theoretical considerations also favor this interpretation; however, we do not feel that the evidence at hand warrants a definite conclusion on this point.

Resumen por los autores, S. R. Detwiler y H. Laurens,
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Estudios sobre la retina.

La estructura de la retina de *Phrynosoma cornutum*.

La estructura general de la retina de *Phrynosoma* es muy semejante a la de la retina de *Chameleon*. Existe un área central muy desarrollada en forma de una convexidad circular situada encima del punto de entrada del nervio óptico, con una fovea que alcanza el máximo de desarrollo en su centro. Un pecten cónico muy vascularizado se proyecta dorso-anteriormente hasta cerca de un milímetro en la cámara posterior del ojo. La retina posee solamente conos, asemejándose bajo este punto de vista a la retina de otros saurios diurnos. Los conos exhiben una variación considerable en tamaño, forma y estructura. Los conos de la fovea están muy atenuados y son cilíndricos, diferenciándose por estos caracteres de los de forma cónica, situados en la región extra-foveal. La presencia de conos dobles no ha podido demostrarse. Bajo condiciones ordinarias de iluminación el pigmento se extiende sobre las células visuales, llegando casi hasta las paraboloideas, excepto en la región de la fovea, en la cual solo los segmentos externos están recubiertos por el.

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STUDIES ON THE RETINA

THE STRUCTURE OF THE RETINA OF PHRYNOSOMA CORNUTUM

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SIX FIGURES

The retina of lizards and turtles is peculiar in that, with few exceptions, it contains only cones. The Gecko, for example (Rochon-Duvigneaud '17), is a nocturnal animal and the pure rod retina which it possesses represents, in accordance with the suggestion put forward by Max Schultze ('66), a retinal mechanism particularly adapted for nocturnal life. According to this widely held view (duplicity theory) pure cone retinæ are indicative of a diurnal mode of life, and forms possessing this type of retina have little or no capability of vision in dim light.

This paper will describe the salient histological features of the retina of *Phrynosoma*, and present a review of the literature in so far as it bears upon the structure of the reptilian retina and the general problems of vision pertaining thereto. The retina of *Phrynosoma* possesses only cones, resembling in this respect the retinæ of other diurnal saurians. In its general make-up it may be said to resemble most closely that of *Chameleon vulgaris* (Garten '07 and Rochon-Duvigneaud '17).

The most striking features which this retina exhibits are: a) the absence of rods; b) the presence of a large conical pecten; and c) the presence of a prominent area centralis containing a maximally developed fovea. A detailed study reveals a number of additional interesting features, the most significant being the shape and structural variableness of the visual elements.

Chievitz ('89, '90, and '91) described the area centralis in a number of representative mammals, birds, reptiles, and amphibians. In the reptiles he found an area in lizards, snakes, turtles,

and crocodiles. According to him, in the Crocodilia (*Crocodylus intermedius* and *Alligator mississippiensis*) it is a simple striped-shaped thickening with a faintly developed fovea in the form of a narrow furrow, running across the retina about 1 mm. from the lower margin of the tapetum. In the turtle, *Emys europea*, the area is a round, thickened region lying above the entrance of the optic nerve, and contains no fovea. In the snake, *Tropidonotus natrix*, Chievitz could not give the exact location of the area because of lack of orientation of the eye; again no fovea could be demonstrated. In *Chameleon vulgaris* the area is described as lying 'behind' the entrance of the optic nerve and containing a deep, highly developed fovea. Rochon-Duvigneaud ('17) also figures a maximally developed fovea in *Chameleon*. In *Lacerta vivipara* and *Lacerta viridis*, Chievitz describes the area as a rounded elevation situated just above the entrance of the optic nerve. Both forms have a slightly developed fovea. Heinemann ('77) could find no fovea in the retinae of Chelonians. Investigation by Detwiler ('16) of several reptilian retinae revealed the absence of a fovea in *Chelopus insculptus* and *Chrysemys picta*, although in both forms an area was found as a slightly thickened region above the entrance of the optic nerve, more highly developed in *Chrysemys* than in *Chelopus*. The retina of the lizard, *Sceloporus undulatus*, showed the presence of a prominently developed area with a deep conical fovea lying above and slightly lateral to the entrance of the optic nerve.

The area-centralis of *Phrynosoma* consists of a doubly-convex circular thickening of the posterior portion of the retina, the vitreal curvature of which is quite marked. It lies above the entrance of the optic nerve (fig. 1) and contains a highly developed fovea (figs. 1 and 2). At its widest portion (including the retinal pigment layer) the area has a thickness of 240 μ ; the retina below the optic nerve at a typical region has a thickness of 150 μ .

Fovea. The fovea is a deep, cone-shaped depression with a broad base, situated in the center of the area (figs. 1 and 3), its apex being about 1.5 mm. above the entrance of the optic nerve. At this point the thickness of the retina (pigment layer included)

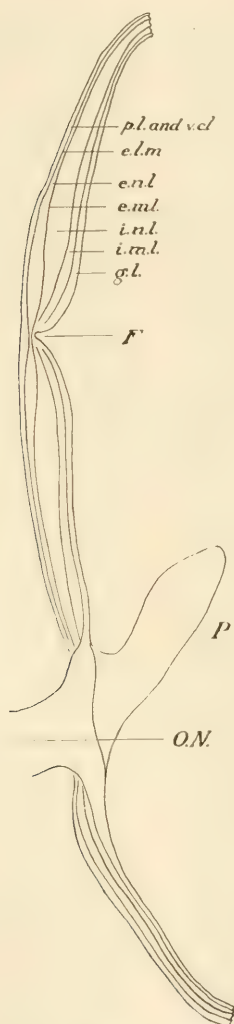


Fig. 1 Camera lucida outline drawing of a sagittal (frontomaxillary) section of the posterior portion of the retina. $\times 30$. *e.l.m.*, external limiting membrane; *e.m.l.*, external molecular layer; *e.n.l.*, external nuclear layer; *g.l.*, ganglionic layer; *i.m.l.*, internal molecular layer; *i.n.l.*, internal nuclear layer; *pl. and v.c.l.*, pigment layer and visual cell layer; *F*, fovea; *P*, pecten; *O.N.*, optic nerve.

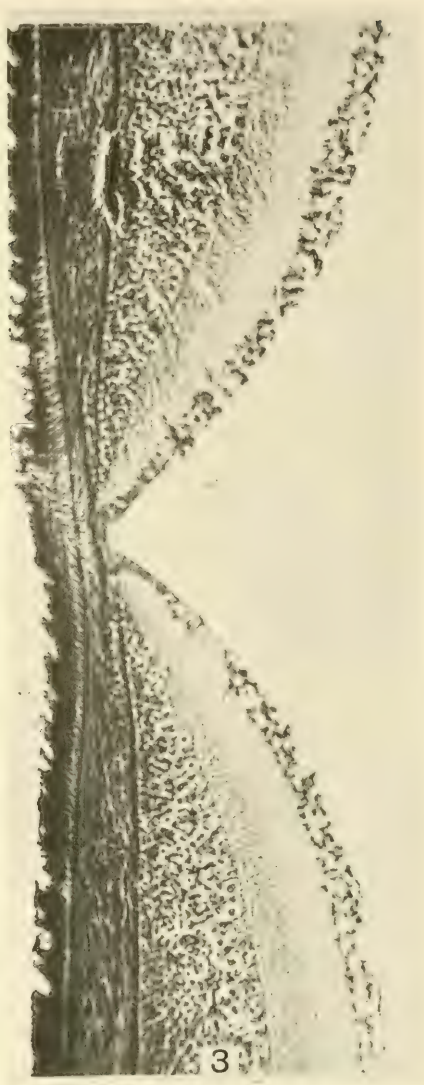


Fig. 2 Photograph of a reconstruction model of the posterior portion of the retina, showing the fovea and the pecten. $\times 20$.

Fig. 3 Photomicrograph of the central portion of the area centralis, showing the prominently developed fovea. $\times 250$. Photographed area = 0.6 mm. in length.

is only $40\ \mu$. Here the retinal layers, which around the periphery of the depression are highly thickened, become greatly thinned out; in fact, at the deepest point of the foveal depression the ganglionic layer, the internal molecular layer, the internal nuclear layer, and the external molecular layer are entirely interrupted, the apex of the depression being surmounted by the external nuclear layer which, at this point, is relatively thin (figs. 1 and 3).

The foveal region shows a marked alteration in the type of visual elements as compared with the remainder of the retina.

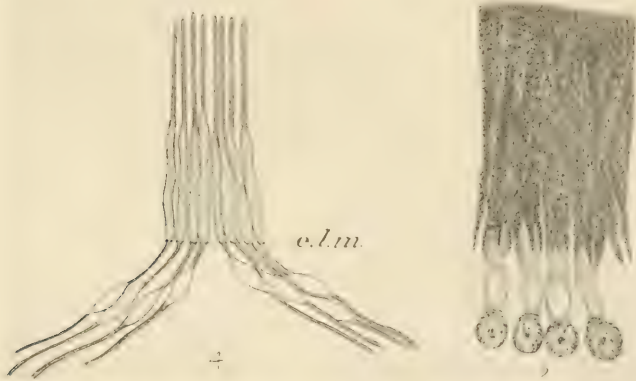


Fig. 4 Diagrammatic drawing of the foveal cones. *e.l.m.*, external limiting membrane.

Fig. 5 A portion of the retina, 1.5 mm. below the entrance of the optic nerve. $\times 935$.

As the fovea is approached the cones become gradually more and more attenuated. Opposite the apex they are so slender that with microscopic magnification of 3000 diameters their width cannot be measured with certainty. Concomitant with these changes is a marked increase in the number of cones and a pronounced thickening of the external nuclear layer which, at its widest portion (about 0.4 mm. from the apex of the fovea), is from eight to ten cell layers thick. At the apex, however, the external nuclear layer is greatly thinned out and is entirely devoid of cone nuclei. The nuclei of the cones of this region lie in a more peripheral position—the cones being connected with their respective nuclei by long attenuated central processes as is illustrated in figure 4.

The increase in the thickness of the external nuclear layer around the periphery of the fovea is accompanied by a corresponding increase in the thickness of the external molecular layer. An examination of figure 3 shows that the greatly thickened internal nuclear and ganglionic layers of the area become gradually thinned out as the foveal depression is approached, and at its apex are entirely wanting.

External nuclear layer. The external nuclear layer beyond the foveal limits consists of only one row of nuclei. Typically, these are rounded or slightly oval in shape and lie just beneath the external limiting membrane (fig. 5). Around the periphery of the fovea where this layer is greatly thickened as a result of the tremendous increase in the number of cones the nuclei, instead of being rounded or oval, become considerably elongated and spindle shaped—the long axis of the nuclei being diagonally directed between the external limiting membrane and the external molecular layer (figs. 3 and 4). The nuclei in this thickened region are not directly applied to the internal surface of the external limiting membrane but lie deeper in, thus leaving a narrow superficial zone between the external limiting membrane and the nuclei which is occupied by processes connecting the cone nuclei with the inner segment.

The presence of only one row of nuclei in the external nuclear layer was found in the eyes of the lizards, *Sceloporus* and *Cnemidophorus* (Detwiler '16). In a pure cone retina, the external nuclear layer is not necessarily composed of only one row. For example, in the turtle (Detwiler *op. cit.*), where only cones occur, the external nuclear layer consists of two rows of nuclei. Chievitz ('89) also found two rows in the eyes of *Emys* and *Lacerta*. He considers the row just internal to the external limiting membrane to be the nuclei of the cones, and the second row to be the nuclei of supporting cells. In the Chameleon eye, Rochon-Duvigneaud ('17) figures but one row of nuclei, while in the eye of the Gecko (which possesses rods only) he shows the external nuclear layer to be several cell layers deep. In the eye of *Alligator mississippiensis* (Laurens and Detwiler '20), the external nuclear layer is double—the outer row being the nuclei of rods, the inner of cones. In the crocodile, Heinemann (77) described

the rod and cone nuclei as occupying a single layer. According to Tafani ('83) the same is true in *Champsia lucius*.

Cones. The cones of *Phrynosoma* exhibit a marked variation in size, shape, and structure, as is illustrated in figures 4 and 6; the cones in the former figure are taken from the fovea. Although there is considerable variability in the shape and structure of the inner segment of the cones outside of the fovea, all are alike in the possession of an oil drop and a rather long conical outer segment. Cones *a*, *b*, *c*, *d*, and *e* (fig. 6) have been taken from a region about 1.5 mm. below the entrance of the optic nerve. Of the different kinds of cones which are typical of this region, types *d* and *e* are the most prevalent. In addition to these



Fig. 6 Selected cones from the extra-foveal portion of the retina. $\times 935$.

types, all of which contain a refractive paraboloid, a number of cones (*f*, *g*, and *h*) without paraboloids have been found. Types *f* and *g* are quite numerous in the region of the retina just below the entrance of the optic nerve, but do not constitute the sole kind of element in this region since types *a* to *e* are present to a variable extent. Cones *f* and *g* were drawn at a distance of $10\ \mu$ from the entrance of the optic nerve. Type *h* (large cones with narrow inner segments and without paraboloids) is infrequent and not characteristic of any particular region.

In the region of the ora serrata, the cones become considerably shortened. The predominant type of visual cell in this region is illustrated by *i* (fig. 6), it is characterized by a broad inner segment with an exceedingly short myoid and a larger paraboloid.

A refractive disc is demonstrable in the inner segment of a large number of the cones, its occurrence having no correlation with the presence or absence of a paraboloid. It is clearly shown in types *c*, *d*, and *e* with paraboloids, and types *f* and *h* without paraboloids. Cones without both paraboloids and refractive discs (type *g*) are rare, and their presence is most common in the region near the entrance of the optic nerve.

A search for double cones has been without success. In a number of regions, types *b* and *g* could be found in rather close relationship, simulating a double cone, but the loose intimacy of the two elements could hardly warrant their being called double. The absence of well defined double cones is in striking contrast with their common occurrence in the retinae of reptiles in general (see Detwiler '16, Laurens and Detwiler '20), but in agreement with conditions in the retina of Chameleon (see Garten '07 and Rochon-Duvigneaud '17), which contains single cones only.

As the fovea is approached the cones gradually become more and more slender and cylindrical in form, accompanied by a loss of the paraboloid bodies and oil-drops. At the apex the visual elements, as above mentioned, are so small and attenuated that their structure cannot be definitely determined by the use of the highest microscopic magnification at our command. Their general shape, in so far as could be determined, is shown in figure 4 and bears a close resemblance to the foveal elements of the human eye (see Schultze '66, fig. 3, Pl. 13).

Pecten. The pecten is a conical shaped structure approximately 1 mm. in length, with its base applied to the inner surface of the optic nerve at its entrance, and its apex projecting dorsally into the posterior chamber of the eye (figs. 1 and 2). It is very vascular; thus indicating its function as a nutritive organ. It is also deeply pigmented—the pigment occurring in the form of minute granules which are scattered throughout the stroma of the organ. In general, in shape and structure, it resembles the pecten found in the eye of *Sceloporus* (Detwiler '16).

The presence of a pecten has been demonstrated in a number of reptilian eyes. Heinemann ('77) found a small pecten in the eyes of several Chelonians. Its presence in the eyes of a number

of American turtles could not be demonstrated (Detwiler '16). Rochon-Duvigneaud ('17) describes it in the eye of Chameleon and of the Gecko as a cone-shaped structure. In Alligator mississippiensis (Laurens and Detwiler '20) it was found to be only slightly developed—being present in the form of a lightly pigmented cap covering the orbital pole of the optic nerve.

Pigment epithelium. The epithelial layer offers no special peculiarities. With the exception of Alligator mississippiensis (Laurens and Detwiler '20) it is not unlike that in other reptiles previously investigated (Detwiler '16). The pigment is extremely abundant and, in addition to occupying finger-like processes embracing the visual elements, is so compact in the cell body as to occlude from view the epithelial nuclei (fig. 5). It is present in the form of delicate brownish needle-like granules which in the cell body proper, are so thick as to form a black pigment mass appearing almost homogeneous. In the vitreal processes, however, it thins out slightly and the separate pigment granules are more clearly discernable.

Under normal conditions of illumination (diffused daylight) the pigment extends down over the visual cells almost as far as the paraboloid, and in some cases to the refractive disc (fig. 5), covering thereby not only the outer segment, but a considerable portion of the inner segment as well. At the apex of the foveal depression the pigment does not extend quite as close to the external limiting membrane as it does more peripheralward (fig. 3), and the entire inner segment is uncovered.

The position of the pigment has not been studied under different conditions of illumination. It is the aim, however, of the authors to investigate this as a sequence to the present paper.

SUMMARY

1. The general structure of the retina of Phrynosoma bears a close resemblance to that of Chameleon.

2. There is a prominently developed area centralis in the form of a circular convexity above the point of entrance of the optic nerve (fig. 1), with a maximally developed fovea at its center (figs. 1 and 3).

3. A highly vascular conical peeten projects dorso-anteriorly about 1 mm. into the posterior chamber of the eye (figs. 1 and 4).

4. The retina possesses only cones, resembling in this respect the retinæ of other diurnal saurians. The cones exhibit a considerable variation in size, shape, and structure (figs. 4 and 6).

5. The cones of the fovea are greatly attenuated and cylindrical in form as compared with the conical form of those in the extra-foveal region (cf. figs. 4 and 5). The presence of double cones could not be demonstrated.

6. The pigment under ordinary conditions of illumination extends down over the visual cells, almost to the paraboloids (fig. 5) except in the foveal region, where only the outer segments are covered (fig. 3).

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interrupted current, and to degrees of temperature between 22°C. and 40°C. In this area are felt only the stimuli affecting the protopathic sensibility, such as the prick of a pin and temperatures below 20°C. and above 40°C.

This seeming dissociation of sensory loss which persists, throughout the time of regeneration of an injured nerve, offers among others two problems. First, the reason for the preservation of certain sensibility in the intermediate zone or that area between the borders of the loss to light touch and the loss to pin prick, and, second, the reason for the increase in size of this area of sensibility as time goes on.

The preservation of sensibility to any type of stimulation within the sensory area usually assigned to a nerve immediately following its section can be due to but one cause, nerve overlap.

The further return of sensibility in the intermediate zone can be due to but two conditions, nerve regeneration or the assumption of function by adjacent nerves. Relative to the possibility of nerve overlap, Head (2) and his co-workers state that "such overlapping should lead to rapid restoration of sensibility to prick, and in some cases possibly forms a factor when sensation returns with unusual rapidity. Commonly no wide loss to prick on the palm follows division of the median nerve, because the fibers which conduct this form of sensation are supplied from both nerves. But supposing the nerve supply of the median palm came overwhelmingly from the median, division of the nerve would produce at first total analgesia. This might rapidly pass away, to some extent, as soon as the few fibers of the ulnar nerve to the median palm became capable of supplying sufficient sensibility for the transmission of impulses." Again they say (page 149) "With so much overlapping of nerve supply, complete recovery of sensibility to prick pain might occur without union of the divided nerve, by a further development of those fibers in the uninjured nerve which normally supply the affected parts. In areas where sensation to prick is only partially lost, such substitution undoubtedly occurs, But there is no evidence to show that restoration of sensation can be produced in analgesic parts without union of a divided nerve."

Finally, they state (page 140) that "Division of the nerve (one of the nerves of the hand) leads at once to the production of an area of absolute cutaneous insensibility, surrounded by an area of loss of sensation to stimuli, such as light touch and the minor degrees of temperature. The relative extent of these two areas differs greatly in each individual case, and the first definite sign of recovery is shown by an increase in size of the intermediate zone between them."

It can be seen that, although it is admitted that some return of sensibility to pin prick may be the result of nerve overlap, the extent of this return and the limit of time wherein this return may take place is not defined. If any overlapping of peripheral nerves is possible it becomes necessary to define the fullest possible extent of this overlap and the limit of time for its occurrence.

It must be emphasized that this problem is not concerned with the question of whether any degree of pain sense is lost throughout the whole area of the accepted sensory distribution of a nerve wherein tactile sense is always lost. Cobb (3) has pointed out again that "by varying the quantitative value for the stimuli, dissociation of sensations can be predicted and produced almost at will;" that by using low degrees of pressure they can obtain charts whereby painful stimuli and tactile stimuli produce co-extensive areas of anesthesia. This would tend to show that pain sense as well as tactile sense is lost in a co-extensive area following division of a mixed nerve. But it must be admitted that even if this is the case, pain sense cannot be entirely lost in the intermediate zone, else painful stimuli with higher degrees of pressure, insufficient to produce pressure pain, would not be perceived. However closely may the analgesia to stimuli to low degrees of pressure correspond to the anatomical distribution of a nerve, the presence of any sensitiveness to pin prick, which is not due to pressure pain, requires explanation.

I maintain that not only the immediate presence, but the return of sensibility to prick pain alike, which occurs before the return of tactile sensibility, occurs in regions which occupy the

area of nerve overlap,¹ and that this return of sensibility to pin prick cannot be interpreted as a sign of nerve regeneration.

I am supported in this view by the facts that I have never found a return of sensibility to pain, when sensibility to touch has not returned, except in an area of overlap; that when a nerve is divided and at the same time one or more adjacent nerves are divided sensation to pin prick does not return in the area of the overlap of these nerves even many months following the injury; that when a nerve adjacent to one which is severed and which supplies an area of overlap to that nerve is sectioned, the preexisting sensibility to pin prick in the overlap area is lost; that when sensibility to pin prick is present in the anatomic distribution of a severed nerve, resection and suture has no effect on the general outline of this area of sensibility.

MATERIAL

My observations were made on 500 patients with peripheral nerve lesions seen early in Base Hospitals in France and 523 patients with peripheral nerve lesions studied later at U. S. Army General Hospital No. 28, Fort Sheridan, Ill.

The observations of early peripheral nerve lesions were in most instances uncontrolled by operative procedures. A large proportion of the lesions were partial and frequently complicated by injuries to adjacent small sensory branches. But these observations served a useful purpose. They showed: 1) that in many cases for the first two or three weeks only a very small area within the border of the part insensitive to cotton wool was sensitive to pin prick; 2) that in a few a larger zone sensitive to pin prick appeared within fifteen days; and 3) that the return to sensitiveness to pin prick in a larger zone, corresponding to the area which we later determined as overlap usually was found, at times variable from thirty to one hundred days. The

¹ By 'overlap' is meant the presence, or assumption of function of sensation by adjacent nerves within the anatomic sensory distribution of a severed nerve. By 'overlap area' is meant that area in which such function is possible through such an agency.

cases showing return to pin prick over a larger area in less than thirty days were predominately cases of radial and musculo-spiral lesions.

The material of peripheral nerve lesions studied later may be divided into two groups: the first, a group of 391 cases of peripheral nerve lesions uncontrolled by operation and in the majority of instances recovering spontaneously; the second a group of 132 cases controlled by operation.

<i>Cases controlled by operation</i>	
<i>Nerve lesions</i>	<i>Number</i>
Ulnar.....	20
Radial.....	31
Median.....	9
Ulnar and median.....	15
Median and radial.....	2
Musculocutaneous, ulnar and median.....	2
Brachial plexus.....	2
Ulnar and radial.....	3
Great sciatic.....	20
External popliteal.....	25
Anterior tibial.....	2
Ulnar, median and internal cutaneous.....	1
Total.....	132

My general impressions relative to the sensory changes in peripheral nerve lesions were derived from the whole material. The areas of overlap were obtained only from cases certified by operation. The cases which have been used in the study of regeneration of nerves likewise were certified by operation. Therefore, although the whole 1023 cases contributed to my general conclusions concerning these problems, only one group, consisting of the cases coming to operation, was employed in obtaining the data which serve as the basis for the special conclusions contained in this article.

METHODS OF INVESTIGATION

The problems under investigation were studied from a clinical and not from a psycho-physical standpoint. The areas of overlap were found in the course of clinical examinations in a large group of cases. The methods of examination, therefore, were

those ordinarily used clinically. The sense of touch was tested by a wisp of cotton. The sensation of pain in response to the prick of a pin was ascertained by using a weighted needle sliding within a bit of glass tubing so that with different weighted needles a pressure of from 5 to 35 grams could be applied.

It must be determined whether these methods are acceptable as to the differentiation of epieritic and protopathic sensibility and deep sensation. Light touch with a wisp of cotton to determine sense of touch may, I think, be accepted if exact threshold of sensation is not under investigation, and if exact borders of loss of sense of touch be not insisted on. For the purpose of this investigation the exact borders of loss of sense of touch need not be insisted on. Only one factor must be considered in this method of examination: namely, return of so-called hair sensibility must not be confused with touch; hence, in testing for touch where an accurate border was to be determined, the parts were closely shaven.

The degree of pressure which it is permissible to employ in determining prick pain without jeopardizing the results by confusion with pressure pain remains to be discussed. Although, as pointed out by Head and Sherren (4), deep sensibility may be evoked when testing for touch with a stiff roll of wool, this objection is not valid for determining prick pain, within certain limits. A sharp needle was used by Head and Sherren in their early clinical investigations, care being taken to differentiate between sense of deep pressure and true pain. Boring (5) says that "In determining the pain threshold it was especially necessary not to exceed pressures of 5 grams. Although at high intensities of stimulus the introspective difficulty of abstracting from pressure was less with pain than with cutaneous pressure, the greater intensities frequently drew blood and therefore were abandoned." As in Boring's work it was necessary to examine a small area of skin repeatedly and at very short intervals for all forms of sensation, his objection is valid. In my case, on the other hand, it was necessary only to examine sense of prick pain in areas of overlap and not to confuse this pain with pressure pain. We have never found pain to result from 35 grams of

pressure with a blunt object, care being taken to obtain from the patient responses only to pain from prick of a sharp point. I believe pressure of even 35 grams to be permissible to map out the overlap of sense of prick pain. No exact measurements of threshold to prick pain were made and in the majority of cases pressure did not exceed 30 grams.

1. USUAL AREA IN WHICH SENSATION TO PIN PRICK RETURNED BEFORE TACTILE SENSIBILITY

For the purpose of this investigation only such cases were selected to illustrate the dissociated return of sensibility to pin prick as were not instances of regenerating nerves. To insure this one of two conditions were insisted on: first the presence of pain sense having been demonstrated within the area of the nerve's supposed anatomic supply, that nerve is found, at operation, to be divided and the ends separated. Second, the nerve having been seen to be divided at operation, presence of pain sense was demonstrated in its distribution within the length of time given for the return of protopathic sensibility as the result of regeneration (Head, Rivers and Sherren, 43 days). In my cases under the second condition 28 days was the limit with the exception of lesions of the radial nerve in which the limit was 37 days.

The areas in which sensibility to pain returns before tactile sensibility are the same under both conditions. It is unnecessary to describe them and they will only be illustrated (figs. 1, 2, 3, 4).

A few conclusions may be drawn from these observations:

1. Following section of a mixed nerve the complete loss of sensibility to pain is far less than the loss of tactile sensibility, which corresponds to the accepted sensory distribution of a nerve.
2. The early and dissociated return of sensibility to pain occurs in certain areas specifically constant for each individual nerve. Inasmuch as in the cases above illustrated, this return of sensation could not have resulted from nerve regeneration it follows that these areas are regions of nerve overlap.
3. The areas in which early return of prick pain was observed

occupied the borders of adjacent uninjured nerves. 4. Some nerves, for example the radial, may have no isolated supply for pain sense.

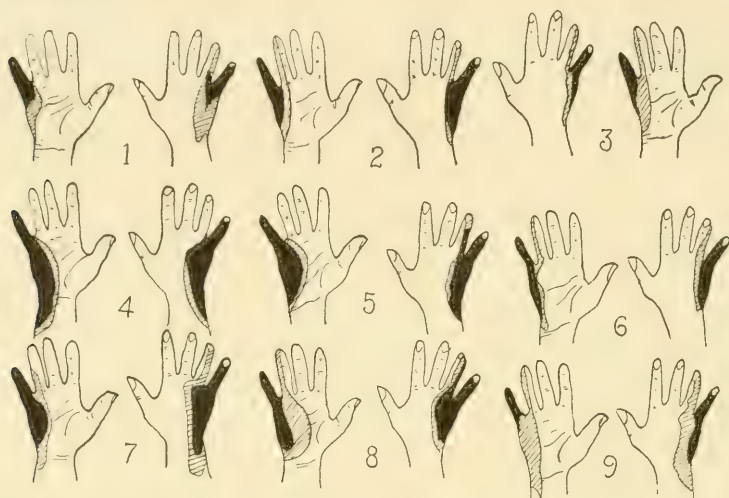


Fig. 1 Sensory loss resulting from complete section of the ulnar nerve. Shaded areas represent loss of tactile sense. Black areas represent loss of pain sense and tactile sense. Numerals refer to case numbers throughout. The algesic areas within the accepted sensory supply of the ulnar nerve are adjacent to the intact median and radial nerves.

1. Y. H. G. S. W. M. G. B. Upper third forearm, July 18, 1918. Operated June 18, 1919. Examined July 21, 1919.

2. J. K. G. S. W. H. E. Above epicondyle, October 4, 1918. Operated March 12, 1919. Examination April 20, 1919.

3. I. W. G. S. W. M. G. B. Upper third forearm, October 10, 1918. Operated September 13, 1919. Examined July 18, 1919.

4. W. S. G. S. W. H. E. Middle third forearm, September 27, 1918. Operated March 24, 1919. Examined April 20, 1919.

5. T. H. G. S. W. H. E. Middle third arm, October 28, 1918. Operated April 1, 1919. Examined April 23, 1919.

6. J. M. G. S. W. H. E. Middle third forearm, September 16, 1918. Operated September 17, 1919. Examined September 1, 1919.

7. C. R. G. S. W. H. E. Upper third forearm, October 11, 1918. Operated March 25, 1919. Examined June 1, 1919.

8. C. N. G. S. W. H. E. Upper third arm, October 17, 1918. Operated April 5, 1919. Examined May 10, 1919.

9. W. P. G. S. W. H. E. Middle third forearm, September 27, 1918. Operated September 6, 1919. Examined September 1, 1919.

G. S. W. = Gun Shot Wound. H. E. = High Explosive. M. G. B. = Machine Gun Bullet.

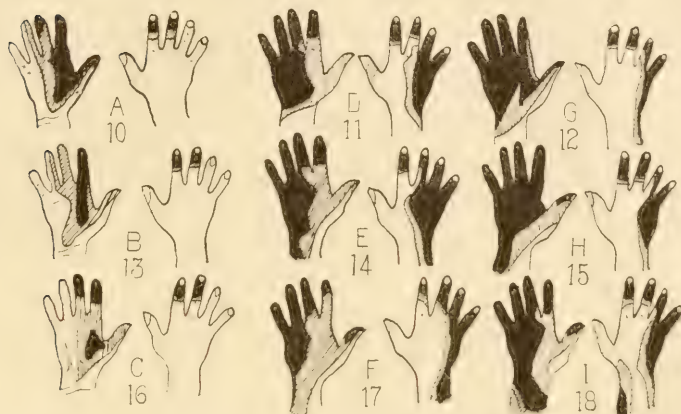


Fig. 2 Sensory loss following complete section of the median nerve, A, B, C; ulnar and median nerves combined, D, G; ulnar, median and internal cutaneous E, F, H; and ulnar, median, musculo-cutaneous, and internal cutaneous nerves, I. Figure C shows in addition to the section of the median nerve slight hypaesthesia over the ulnar distribution due to a minor lesion of the ulnar nerve. Figure I represents the sensibility remaining in the hand after all the nerves with the exception of the radial, supplying sensation to the hand, have been severed. It follows that the radial nerve overlaps on to the palm to a large degree.

10. V. A. G. S. W. H. E. Lower third arm, September 28, 1918. Operated May 21, 1919. Examined May 5, 1919.

11. B. W. G. S. W. H. E. October 11, 1919, upper third forearm. Operated April 18, 1919. Examined April 18, 1919.

12. G. P. G. S. W. M. G. B. Lower third arm, October 31, 1918. Operated May 29, 1919. Examined May 17, 1919.

13. R. A. G. S. W. H. E. Right elbow, August 4, 1918. Operated May 5, 1919. Examined May 31, 1919.

14. G. P. G. S. W. H. E. Middle third arm, October 4, 1918. Operated April 5, 1919. Examined April 1, 1919.

15. V. Q. G. S. W. H. E. Middle third arm, November 10, 1918. Operated April 19, 1919. Examined May 29, 1919.

16. T. P. G. S. W. H. E. Upper third forearm, November 1, 1918. Operated May 27, 1919. Examined May 2, 1919.

17. A. B. G. S. W. H. E. Upper third arm, July 6, 1918. Operated May 6, 1919. Examined May 30, 1919.

18. W. R. G. S. W. H. E. Lower third arm, July 15, 1918. Operated June 29, 1919. Examined June 23, 1919.

2. EFFECT OF SIMULTANEOUS SECTION OF ADJACENT NERVES UPON RETURN OF PAIN SENSIBILITY

If the shrinkage of the area insensitive to pin prick, responsible for the increase in size of the intermediate zone, be a sign of nerve regeneration and not a result of overlap, it should occur whether the adjacent nerves be affected or not. This, however, is not the case, as will be shown. In other words, if certain

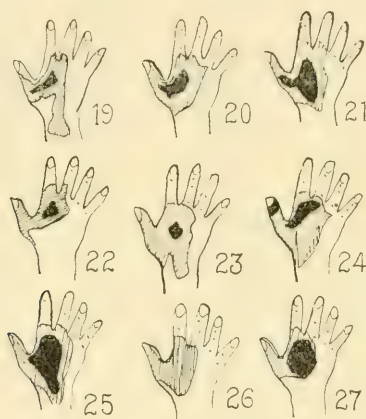


Fig. 3 Sensory loss resulting from complete section of the radial nerve. No. 26 illustrates that no analgesia may result.

19. M. S. G. S. W. M. G. B. Middle third arm, November 10, 1918. Operated May 21, 1919. Examined May 5, 1919.

20. P. J. G. S. W. H. E. Upper third arm, September 28, 1918. Operated May 16, 1919. Examined May 13, 1919.

21. H. J. G. S. W. H. E. Lower third arm, October 20, 1918. Operated June 3, 1919. Examined May 23, 1919.

22. B. J. G. S. W. M. G. B. Middle third arm, October 8, 1918. Operated March 22, 1919. Examined April 17, 1919.

23. G. W. G. S. W. H. E. Middle third arm, October 31, 1918. Operated March 17, 1919. Examined April 28, 1919.

24. D. G. G. S. W. M. G. B. Upper third arm, October 26, 1918. Operated April 15, 1919. Examined May 18, 1919.

25. W. L. G. S. W. H. E. Upper third arm, October 31, 1918. Operated May 6, 1919. Examined May 1, 1919.

26. E. F. G. S. W. H. E. Upper third arm, November 10, 1918. Operated May 8, 1919. Examined June 17, 1919.

27. C. F. G. S. W. H. E. Upper third arm, November 7, 1918. Operated April 22, 1919. Examined May 6, 1919.

areas of skin become sensitive to pain or are found sensitive to pain following section of a given nerve, and the condition is due to nerve regeneration, then simultaneous section of an adjacent



Fig. 4 Sensory loss resulting from complete section of the external popliteal nerve. The algesic areas within the accepted sensory distribution of the nerve are found adjacent to the areas supplied by the intact internal popliteal and internal saphenous nerves.

28. H. E. G. S. W. H. E. Upper third leg, November 4, 1918. Operated May 8, 1919. Examined April 11, 1919.

29. K. G. G. S. W. M. G. B. Upper third leg, October 14, 1918. Operated May 26, 1919. Examined June 30, 1919.

30. S. F. G. S. W. M. G. B. Lower third thigh, August 18, 1918. Operated May 5, 1919. Examined April 28, 1919.

31. K. J. G. S. W. H. E. Knee, October 14, 1918. Operated May 5, 1919. Examined April 28, 1919.

32. N. M. G. S. W. M. G. B. Upper third leg, June 24, 1918. Operated April 24, 1919. Examined June 15, 1919.

33. S. W. G. S. W. H. E. Middle third thigh, October 3, 1918. Operated June 23, 1919. Examined July 29, 1919.

nerve would have no effect on the appearance of this sensibility. What are the facts?

Although in isolated lesions of the ulnar nerve sensibility to pain is frequently seen on the ulnar half of the ring finger, this is never observed when a median nerve is divided at the same time (figs. 2, D, E, F, G, H, I). When the ulnar, radial and median nerves are divided, a year may follow their division and no shrinkage of analgesia be found on the palmar or dorsal surface of the hand, except on the proximal portion of the analgesia where the musculocutaneous and the antibrachii posterior areas adjoin the analgesic area (fig. 5, A, B, C). When a radial lesion is combined with a median analgesia is always present on the radial part of the palm (fig. 5, D, E, F, G). When a median lesion or a radial lesion alone is present, this part of the palm is usually sensitive to pin prick. Isolated lesions of the external popliteal nerve may show only a small area of analgesia, but when the internal popliteal as well as the external popliteal is severed, there is never found any shrinkage of analgesia or reappearance of sensibility to prick pain in the zone where the supply of the external popliteal meets that of the internal popliteal (fig. 6)

I think it can be definitely stated that when nerves supplying adjoining areas are severed, sensation to pain is at no time present in the border areas, where it is uniformly observed when either nerve is divided alone (fig. 7).

Inasmuch as a large number of my cases have had resections and sutures performed at least three months prior to the last examination, it may be stated likewise that no sensation to pain returned in such areas in the time given for the beginning of regeneration of protopathic sensibility.

3. EFFECT OF SUBSEQUENT SECTION OF AN ADJACENT NERVE UPON SENSIBILITY TO PAIN IN THE AREA OF A SEVERED NERVE

When return to sensibility to pain or presence of sensibility to pain is found in the area of overlap of an adjacent nerve, analgesia will result if this nerve is severed.

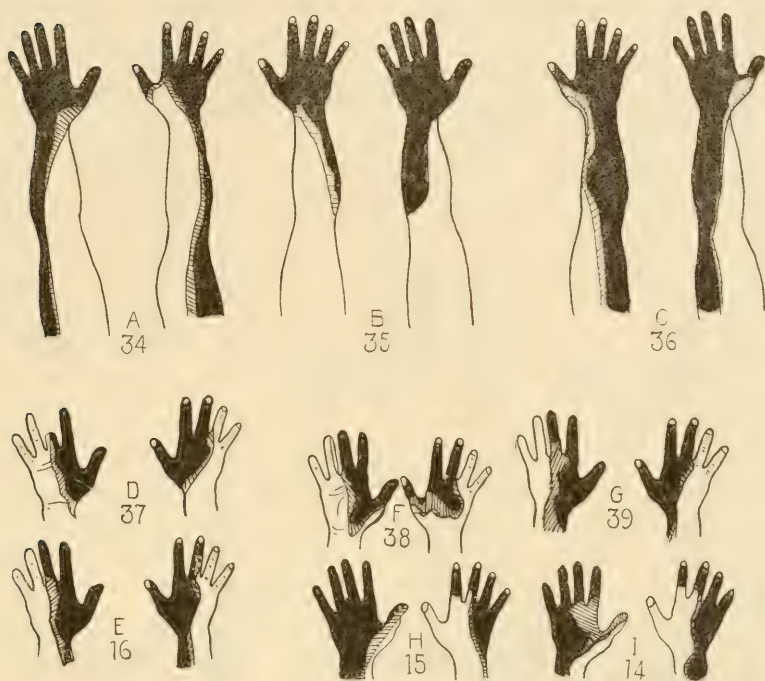


Fig. 5 Sensory loss resulting from simultaneous section of more than one nerve. Figure A, ulnar, median, radial, internal cutaneous, and lesser internal cutaneous. Figure B, ulnar, median, radial, and internal cutaneous. Figure C, ulnar, median, musculo-spiral, internal cutaneous, and lesser internal cutaneous. Figure D, E, F, G, radial and median. Figures H, I, ulnar and median. In no instance is there return of pain sensibility upon the borders between the sensory distribution of the several severed nerves.

34. G. F. G. S. W. H. E. Axilla, October 17, 1918. Operated May 24, 1919. Ulnar and median nerves divided. Musculo-spiral constricted and imbedded in scar. Examined August 7, 1919.

35. B. J. G. S. W. H. E. Axilla, September 6, 1918. Operated May 24, 1919. Examined May 22, 1919.

36. Y. E. G. S. W. H. E. Axilla, July 15, 1918. Injury as above. Operated April 17, 1919. Examined July 8, 1919.

37. S. A. G. S. W. H. E. Middle third forearm, October 16, 1918. Operated March 12, 1919. Examined June 5, 1919.

38. H. W. G. S. W. H. E. Elbow, October 12, 1918. Operated March 18, 1919. Examined July 20, 1919.

39. M. Lt. G. S. W. H. E. Upper third forearm, July 14, 1918. Operated February 6, 1919. Examined May 3, 1919.

14. Examined May 29, 1919.

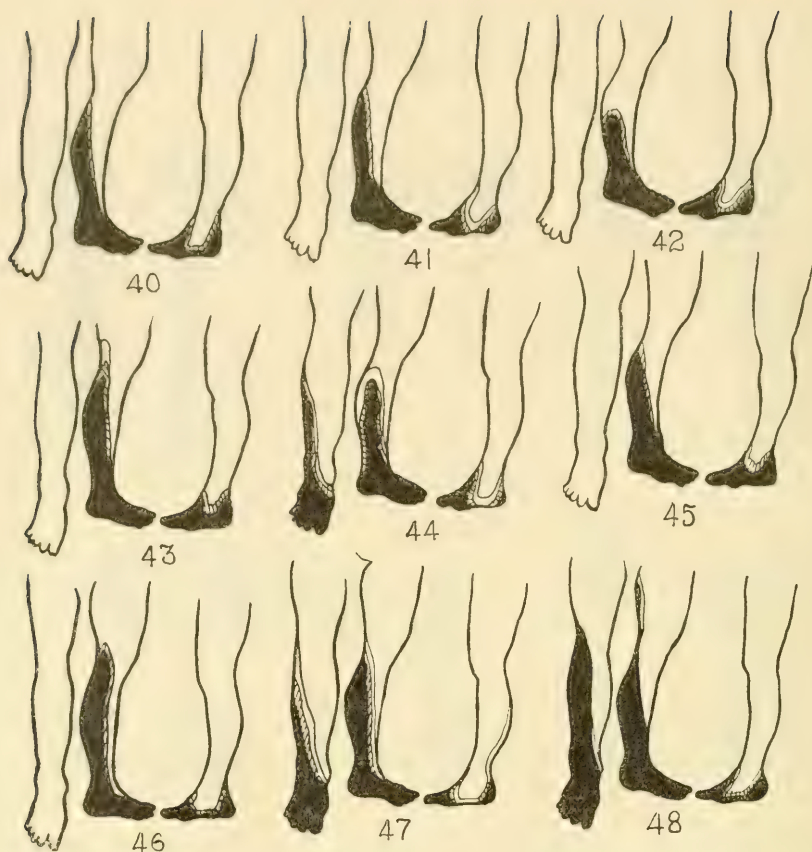


Fig. 6 Sensory loss resulting from simultaneous section of the internal and the external popliteal nerves. No algesic zone can be found between the areas supplied by these two nerves.

40. L. J. G. S. W. H. E. Middle third thigh, September 22, 1918. Operated March 19, 1919. Examined May 6, 1919.

41. S. H. G. S. W. H. E. Lower third thigh, October 4, 1918. Operated July 8, 1919. Examined May 5, 1919.

42. W. P. G. S. W. M. G. B. Middle third thigh, July 31, 1918. Operated May 19, 1919. Examined May 3, 1919.

43. D. C. G. S. W. M. G. B. Middle third thigh, October 1, 1918. Operated April 1, 1919. Examined May 20, 1919.

44. H. C. G. S. W. H. E. July 19, 1918, lower third thigh. Operated January 27, 1919. Examined June 13, 1919.

45. L. G. G. S. W. H. E. Middle third thigh, October 10, 1918. Operated May 16, 1919. Examined July 10, 1919.

46. L. H. G. S. W. H. E. Upper third thigh, October 9, 1918. Operated April 7, 1919. Examined May 17, 1919.

47. L. H. G. S. W. H. E. Upper third thigh, October 9, 1918. Operated April 7, 1919. Examined July 7, 1919.

48. H. S. G. S. W. H. E. Right buttock, July 18, 1918. Operated July 8, 1919. Examined May 17, 1919.

In a case wherein a partial ulnar lesion was combined with a complete section of the median nerve prick pain was preserved in the radial portion of the palm and index finger. When at operation the superficial radial nerve was resected for use as a cable transplant, this part of the palm became analgesic (fig. 8, A, A'). This proves that what sensation was present in the radial portion of the palm and index finger was subserved by the radial nerve.



Fig. 7 Illustrating, A, the usual area in which pain sensibility returns before tactile sensibility when the external popliteal nerve is severed alone; B, the ulnar alone; C, the radial alone. In Figure D, the shaded area represents that return of pain sensibility in isolated section of the median nerve, due to ulnar overlap; the black area that due to radial overlap.

In cases of complete section of the ulnar nerve where the superficial radial nerve was severed to be used as a cable transplant, the preexisting sensibility to pain on the radial border of the sensory supply of the ulnar nerve disappeared, proving that this sensibility was subserved by the radial nerve (fig. 8, B, C, D, B', C', D').

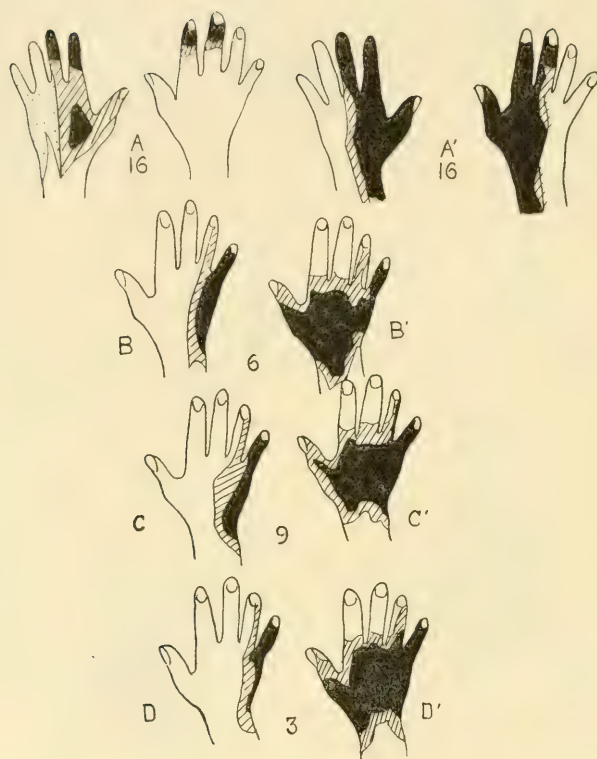


Fig. 8 A, represents the sensory loss resulting from a complete section of the median nerve and a minor lesion of the ulnar. A', when the superficial radial nerve was subsequently severed the preexisting sensibility of the radial side of the palm disappeared. B, C, D, represent the sensory loss on the dorsum of the hand resulting from complete section of the ulnar nerve. B', C', D', when the superficial radial nerve was severed subsequently to be used as a transplant, the algesic area found within the sensory distribution of the ulnar nerve, disappeared.

16. A'. Superficial radial nerve used as cable transplant in operation May 27, 1919. Examined June 3, 1919.

6. Superficial radial nerve used as transplant September 17, 1919.

B'. Examined September 25, 1919.

9. Operated September 6, 1919. Examined September 25, 1919.

3. Operated September 3, 1919. Examined September 25, 1919.

4. EFFECT OF RESECTION AND SUTURE ON SENSIBILITY OF AREA IN WHICH THERE HAS BEEN DISSOCIATED RETURN OF SENSIBILITY TO PAIN

The conditions necessary to study profitably the effect of resection and suture of nerves on return of sensibility to pain are: first, that the nerve ends be separated and, second, that the examination subsequent to operation be made within the period of time ascribed to the return of protopathic sense as the result of regeneration.

Some difficulty is encountered in meeting the second condition, inasmuch as frequently the wide separation of the ends of the nerves makes it necessary to place the extremity in a position which will permit approximation, and to fix it in such a position by means of a cast. This often prevents an examination before six weeks have elapsed. None of the cases here reported were examined later than fifty days after operation, one in less than fifteen days. Although some objection may be made to the cases examined over forty-five days after operation on the grounds of beginning return of protopathic sense due to regeneration, the similarity of the areas unaffected by operation in cases examined under forty-five days and those between forty-five and fifty, coupled with the fact that the ends of the nerves were separated in all of these cases, makes it reasonable to admit them into the group.

The areas which are sensitive to pin prick in the lesions examined, and the sensory changes following operation need only be illustrated. It is sufficient to state that the following nerves were studied: ulnar, examined forty-two days after operation; ulnar and median, forty-five, thirty-six, forty, forty-six, forty-eight and fourteen days after operation; external popliteal, forty-eight, thirty-six, twenty, and twenty-six days after operation; sciatic, fifty and thirty-six days after operation (figs. 9 and 10).

Following resection and suture when sensibility to pain is present in an area of overlap, although some change in the outline of this area occurs, in general the area remains the same.

Head and Sherren (6) state that "Sometimes it is necessary to divide an injured nerve, after sensibility to prick has already begun to return to the hand, that more perfect union may be obtained. Wherever such an operation has been performed, the parts that had begun to recover sensibility became again insensitive to prick, a proof that the recovery must have been due to union, however imperfect, of the divided nerves." In such cases as show return of sensibility to pain as the result of actual regeneration, subsequent resection would be expected to produce analgesia. Similarly, the existence of sensibility to pin prick in a partially severed nerve would be destroyed if that nerve be resected. The whole area of the anatomic sensory supply of a nerve must be rendered analgesic following resection before it can be stated that no part of the return of sensation was due to overlap. In all of my cases, dissociated return of pain sense occurred within the area of nerve overlap and remained intact following resection and suture. Nowhere have I found an illustration of dissociated return of pain sense except in such an area of overlap.

DISCUSSION

1. The preceding observations show that the dissociated return of sensibility of cutaneous pain occurs only in areas of possible overlap.

2. When several nerves serving adjacent areas are severed simultaneously, sensibility to cutaneous pain is not present after

Fig. 9 Sensory changes before and after resection and suture of various peripheral nerves. A, before, A', after resection and suture of the ulnar nerve. B, D, E, before, B', D', E', after resection and suture of the ulnar and median nerves in cases with additional lesions of the internal cutaneous. G, before, G', after resection and suture of the ulnar and median nerves. H, before, H', after resection and suture of the ulnar, median, and musculo-cutaneous nerves. F, before, F' after resection and suture of the median.

A. Examined July 21, 1919; operated June 8, 1919; A' July 21, 1919.

B. Examined April 5, 1919; operated April 4, 1919; B' May 29, 1919.

D. Examined May 17, 1919; operated May 29, 1919; D' July 8, 1919.

E. Examined April 1, 1919; operated April 5, 1919; E' May 29, 1919.

F. Examined May 5, 1919; operated May 21, 1919; F' June 1, 1919.

G. Examined April 18, 1919; operated April 18, 1919; G' May 30, 1919.

H. Examined June 23, 1919; operated June 29, 1919; H' July 11, 1919.

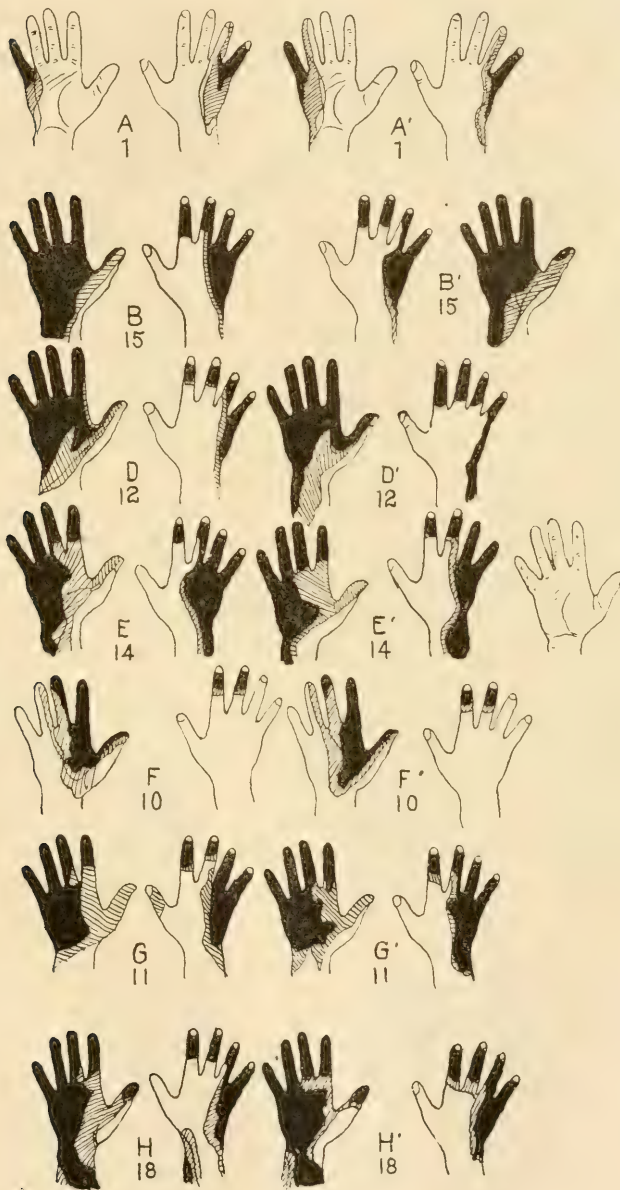


Fig. 9

injury, nor does it return before tactile sensibility in the borders between these areas where it is usually present when either nerve is severed alone.

3. When a region in the area of sensory distribution of a severed nerve is sensitive to cutaneous pain, and the region is adjacent to another nerve area, if this nerve be severed complete analgesia results in the previously sensitive region.

4. When sensibility to prick pain is present or returns in the area of possible overlap on to the sensory distribution of the severed nerve, subsequent resection and suture of this nerve does not change the general extent of this sensitive area, although the borders may at times be slightly enlarged or diminished. That is, the pain sense returned or present before the operation was not due to partial regeneration.

Because of these observations I believe that the early and dissociated return of pain sense attributed by Head to the lawless regeneration of protopathic sensibility is due to the assumption of function of adjacent and overlapping nerves.

It may still be contended that although the early return of prick pain is due to nerve overlap, it is this type of sensation which Head designates as protopathic. In other words, we are still confronted with the possible existence of two distinct systems of fibers for cutaneous sensibility. This is true, but one of the most important links in the theory advanced by Head was the temporal dissociation of the regeneration of the two types of sensory fibers. At least this part of the theory can be justly criticized.

Fig. 10 Sensory changes before and after resection of the K, F, sciatic nerve and A, B, C, G, external popliteal nerve.

K. Examined June 16, 1919; operated July 21, 1919; K' July 29, 1919.

C. Examined May 30, 1919; operated July 7, 1919; C' July 29, 1919.

G. Examined May 15, 1919; operated June 4, 1919; G' July 22, 1919.

A. Examined May 30, 1919; operated July 9, 1919; A' August 9, 1919.

F. Examined June 29, 1919; operated June 23, 1919; F' August 29, 1919.

B. Examined June 5, 1919; operated May 1, 1919; B' May 31, 1919.

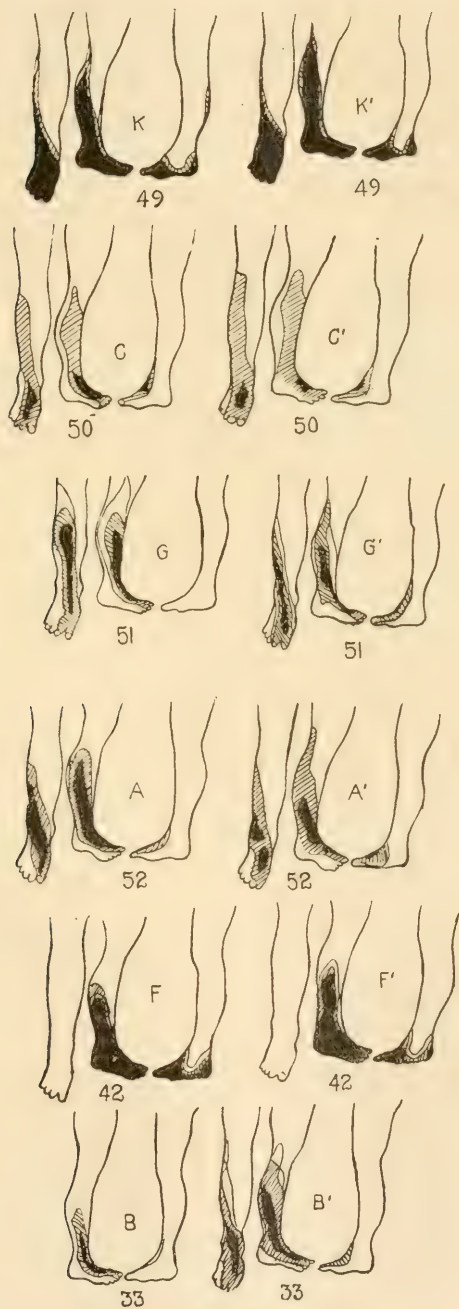


Fig. 10

It is reasonable to assume that the imposed necessity for function of adjacent overlapping nerves should be manifested by the assumption of the less differentiated types of sensation which are of a protective nature. The extent to which overlapping nerves may be educated can only be determined by further psycho-physical study.

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Resumen por la autora, Mabel Bishop,
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El sistema nervioso de un embrión bicéfalo de cerdo.

El presente trabajo es un estudio detallado del sistema nervioso de un embrión de cerdo, bicéfalo y simétrico, de 22 mm. de longitud, con especial mención del sistema nervioso al nivel de la cabeza y cuello. En dicho estudio se incluyen descripciones de los nervios espinales cervicales y tronco del simpático, los ganglios craneales del simpático, nervios craneales, cerebro y tractos fibrosos en vías de desarrollo. Una introducción que contiene unas pocas reflexiones sobre el valor del estudio de casos teratológicos que ocurren libremente en la naturaleza en su relación con la teratología experimental y la embriología normal, precede a la parte descriptiva del trabajo.

Translation by José F. Nonidez
Cornell Medical College, New York

THE NERVOUS SYSTEM OF A TWO-HEADED PIG EMBRYO

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TWENTY FIGURES

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INTRODUCTION

The present investigation was stimulated by an earlier comparative study of the circulatory system in young teratological specimens of the laterally symmetrical dicephalous type occurring free in nature (Bishop, '08). This was an intensive study of a single system, chosen because it appears early in embryonic life,

is functional from its beginning, and readily reflects developmental changes.

In it certain findings irrelevant to the subject then under consideration raised sundry questions that fostered further investigation. Moreover, a review of teratological literature revealed the fact that, excluding experimental teratology, most studies of terata were superficial or fragmentary and confined largely to human abnormalities, which were described primarily because they were 'monstrosities.' The other outstanding facts were that, 1) detailed studies of individual embryos and foetal terata were few and comparative studies of such material rare, Gemmill ('01, '03), Schwalbe ('06, '07), and Kaestner ('07) having given probably the best contributions up to the time of Mall ('08) and Wilder ('08); 2) in the same category there was included more or less indiscriminately every kind of creature whose body was not moulded after the average pattern of its respective species.

The examination of various terata, supplemented by much reading, has added my emphasis to that of others that a sharp distinction ought to be made between terata that are pathological (i.e., those in which degenerative processes predominate) and orderly developed, symmetrical organisms whose 'monstrosities' appear to consist primarily in a regulatory adjustment to physiological conditions (i.e., regulatory processes predominate) whether or not these be due to factors known or still speculative. That the term 'Cosmobia' suggested by Wilder ('08) be adopted to designate these orderly developed terata is of minor importance, but to make the discrimination is not a mere quibble of classification, it seems to me, but rather the recognition of two distinct anatomical and physiological conditions having equally distinct scientific value.

Behavior studies of terata are also unsatisfactory in that they have been made from a spectacular point of view, largely because the creatures (mostly human) were exploited 'freaks,' such as the Siamese twins, the Tocci brothers, the Hungarian sisters Helen and Judith, and others. Barbour ('96) studied in a far more scientific spirit the daily behavior of a symmetrical two-headed tortoise from about the second day after hatching in June up to its

death by accidental injury in September. Had he followed this by a gross and microscopical study of the nervous system, its scientific value would have been manifestly increased.

I believe the time is not yet ripe for a final valuation of teratology, since a more complete study of the internal anatomy of terata after birth or hatching is needed, preceded in so far as possible by careful observations of their behavior and physiology, for external forms shed little light upon structures within, and in almost every case of symmetrical double monsters, at least, the duplicity is greater internally than externally. Detailed studies of each system through a series of developmental stages in embryos and foetuses of the same type of abnormality, followed by comparative studies of the same stages in several types, are of especial value, since the modifying influences undoubtedly occur in embryonic life. And if such embryos occurring free in nature are of true scientific value they should serve as a control for experimental teratology and be capable of correlation not only with this aspect of the teratogenetic problem, but also with the whole scheme of the mechanics of normal development. Until a large body of such data on free-in-nature embryos has been recorded, I believe that the final evaluation of teratological studies, especially of teratembryology, cannot be given.

Since intensive studies of the central nervous system have been especially neglected, the present investigation places on record the data gathered from a detailed study of this system in a young mammalian embryo in accordance with the programme suggested. No attempt has been made to add another review of the voluminous literature on teratology, or to enter into a discussion of the causation of abnormalities.

DESCRIPTION OF THE MATERIAL

The specimen studied is a two-headed pig embryo, 22 mm. in length, bilaterally symmetrical and well developed. Before being loaned to me for study, it had been cut into an almost perfect series of cross-sections, each 20 μ in thickness, and stained with Delafield's hematoxylin and eosin. As I had not seen the specimen in toto, a wax-plate model of the embryo rostral to the

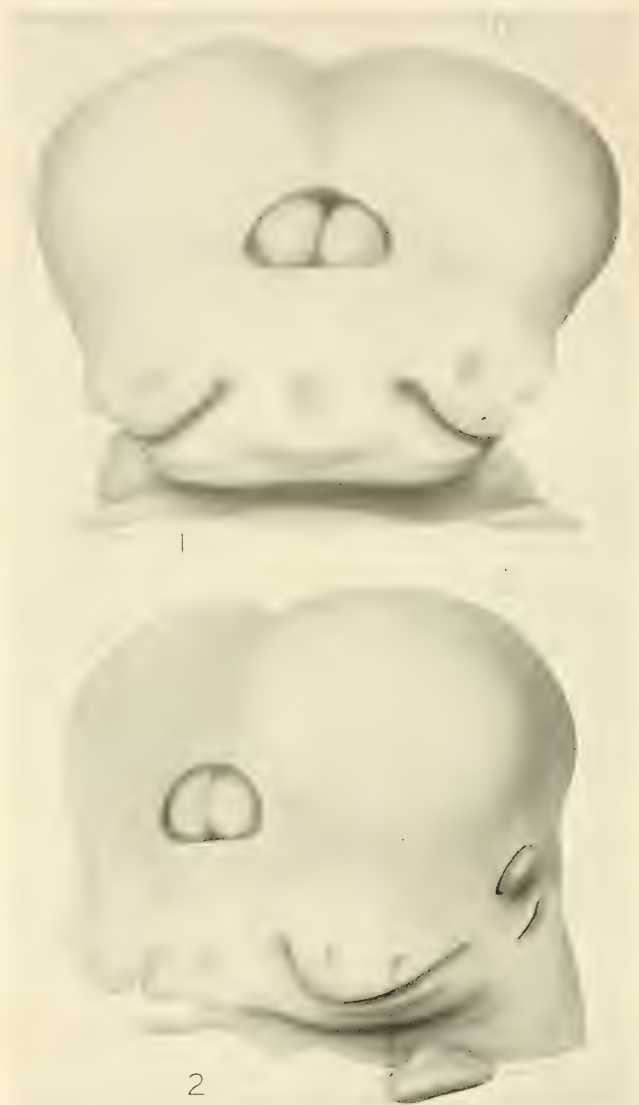


Fig. 1 Front view of the model of the teratological head. This shows the bilateral symmetry of the head, the median eyes, and below them in the midline, a depression which is a median (conjoined) external auditory meatus. The area between the snouts is a mandibulomaxillary complex containing structures of the left half of head A and the right half of head B, some of them conjoined, some not. The embryological neck bend is shown in deep shadow, and below it the anterior limb buds. $\times 25$.

Fig. 2 Frontolateral aspect of the same model. This shows head A in profile from its left side, and head B in full-face view. $\times 25$.

anterior limb buds was made in order to understand clearly the morphological axes and planes of section. The model conforms accurately to the external appearance of the teras already described and figured (Wilder, '08; Bishop, '08), but to bring the organism quickly before the reader Wilder's pen sketches have been reproduced, and two drawings of the model added (figs. 1, 2, 3).

Below the level of the shoulders the embryo appears externally as a single individual arising from one umbilical cord. The head region, however, is partly double. The snouts are separate

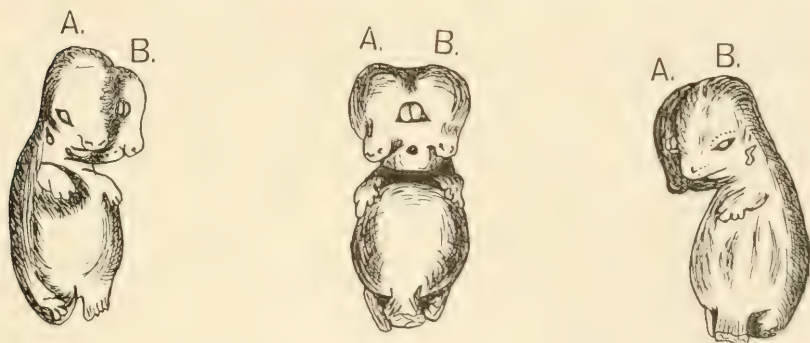


Fig. 3 Three pen-and-ink sketches of the entire embryo made before it was sectioned. (After H. H. Wilder.)

and diverge at the same angle from the median plane of the organism, although the doubled head is twisted a little to the left, and the right member (designated head A) is tilted downward slightly more than the left (head B). Above and between the diverged snouts there is a single palpebral opening in which are two separate eyeballs, the left eye of one member being approximated to the right eye of the other. Because of the tilting of heads A and B, the median eyes lie at a higher level than the outer eyes.

The outer sides of the teratological head appear normal in every respect (figs. 2, 3). Below these median eyes and between the diverged snouts is a broad area which externally has little to commend it to the reader's attention, but internally its anatomy showed it to be one of the most interesting regions of the entire

embryo and it has been given special attention. It consists of the joined left half of head A and the right half of head B and is, therefore, a mandibulomaxillary complex with contributions from both heads. Since its structures are intimately concerned with the identification of the median isolated ganglion, its internal anatomy is discussed in that connection (p. 411). Throughout the embryo the duplicity of the teras is more apparent internally and greatest in the head region.

METHOD OF STUDY AND TERMINOLOGY USED

A careful study of the anterior five hundred sections has been made, therefore, with special reference to the nervous system in the head and neck. A wax-plate model of the brain, spinal cord, and nerves in these regions was made as follows: Beginning with section 500 and using every alternate section cephalad, all parts of the nervous system visible under low-power objective of the compound microscope were magnified twenty-five diameters and projection lantern drawings made. These were transferred to wax plates 1 mm. in thickness, and the model stacked in segments in such manner that it could be readily assembled. Later it was cut through the median sagittal plane so as to afford a median aspect of the brain and spinal cord (fig. 5). In stacking, the segments were checked up by rereadings of the microscopical sections and each nerve painted a different color. Black plates were used to indicate every tenth section. The study has been further checked by constant reference to serial sections of normal pig embryos loaned by Prof. F. R. Lillie, of the Department of Zoology of the University of Chicago, and by such references in the literature as had any bearing upon the subject.

Terminology. Before giving a description of the structural conditions found in the teratological embryo, it seems advisable to make clear the terminology used and to call attention to certain points of morphology that are important in interpreting the sections.

For the sake of simplicity, the two members of the teratological head are designated *head A*, the right member; *head B*, the left member. *Teratological head* includes both members and refers to

the head of the embryo treated as a unit. Considering the organism as a single symmetrical solid, the term *median* is used with reference to the brain structures between the raphés of the two heads, or to structures outside of the brain that lie in the area between the diverged snouts. *Inner side* and *outer side* refer to the two sides of each head, e.g., the 'outer side of head A' would be its right side, the 'inner side of head A' its left side. *Normal sides* refer to the outer sides of the heads in contradistinction to the median area. *Rostral* structures are those toward the snout end of the organism; *caudal* (or *caudad*) toward the tail. *Conjoined* structures are those containing contributions from both members. *Dorsal* and *ventral* refer to the back and ventral (belly) sides, respectively. In the description of the nervous system the *sulcus limitans* is taken as the boundary between the dorsal and ventral quadrants.

Among the more important morphological points to be kept in mind are the embryological flexures, which are at their maximum, the axes and planes of the teras as a unit, and the normal morphological axes and planes of each head. For example, there are in reality three median sagittal planes, one for the embryo as a whole and one for each head. To avoid confusion, the latter is referred to as the 'median plane of head A' or 'median plane of head B,' whereas 'median plane' is restricted to the median sagittal plane of the monster as a whole.

The median plane of the monster represents juxtaposed external surfaces of the two heads, i.e., the left side of head A is approximated to the right side of head B. This relationship is of great importance in interpreting the structures in the median region of the organism, the region of greatest interest.

Because head A is tilted downward slightly more than head B, and the top of head B consequently appears higher, the plane of a cross-section in a given region does not always pass through the same structures in the two heads. This gives a false impression of asymmetry. For example, owing to this tilting, the outer eye of head A lies somewhat caudad to that of head B and a section cutting through the middle of the lens of B passes just rostral to the lens of the outer eye of head A (figs. 14, 15). Sec-

tion planes pass through the inner eye of each head before cutting through the outer eye of the same head, since the median eyes lie at a higher level. The obliquity of the inner eyes compared with each other is almost negligible (fig. 10). The forebrains are cut more or less obliquely, owing to the variations in the level of the two heads. Other slight obliquities also occur because of the embryonic flexures, which cause confusion in interpretation unless kept constantly in mind.

EXPLANATION OF FIGURES

Figures 1, 2, 4, 5, and 6 are drawings by A. B. Streedain from wax-plate reconstruction models made by the author. Upon the perpendicular at the right of figure 4 is indicated in arabic numerals the level of the sections of the embryo represented in figures 8 to 20. These figures were made with an Edinger projection lantern and are arranged in serial order. Figure 3 is a free-hand copy of Wilder's pen-and-ink sketches of the embryo before it was sectioned. Cartilage is represented in solid black, muscles by heavy dashes, and nerves in stipple. *A* or *B*, designating the members of the teratological head, and *rt* (right) or *lt* (left) have been added to abbreviations of structures wherever it seemed that ambiguity might otherwise exist. Structures of the median region containing a contribution from both members are referred to as conjoined (*co*) or median. Magnification of all figures, except figure 3, $\times 25$.

ABBREVIATIONS

<i>A</i> , head A	<i>d.fu.</i> , dorsal funiculus
<i>a</i> , artery	<i>Dien.</i> , diencephalon
<i>Alb.gr.</i> , alveololabial groove	<i>E.</i> , eye
<i>All.gr.</i> , alveololingual groove	<i>E.a.me.co.</i> , conjoined (median) external auditory meatuses
<i>Apx.lat.r.</i> , apex of the lateral recess	<i>Epg.</i> , epiglottis
<i>Aq.Syl.</i> , aqueduct of Sylvius	<i>Esoph.</i> , esophagus
<i>B</i> , head B	<i>Ex.a.me.</i> , external auditory meatus
<i>b.vb.</i> , body of a vertebra	<i>Ex.a.me.co.</i> , conjoined (median) external auditory meatuses
<i>C.c.nm.</i> , caudal cranial nerve-mass	<i>Ex.nr.</i> , external nares
<i>Cerb.</i> , cerebellum	<i>Ex.pl.m.</i> , external pterygoid muscle
<i>Cer.hem.</i> , cerebral hemisphere	<i>Fb.</i> , forebrain
<i>Cer.ped.</i> , cerebral peduncle	<i>Fc.l.md.</i> , fasciculus longitudinalis medialis
<i>Cg.e.a.m.</i> , cartilage of external auditory meatus	<i>F.olf.</i> , fila olfactoria
<i>Cg.e.a.m.co.</i> , conjoined (median) cartilages of external auditory meatuses	<i>G.g.</i> , gasserian ganglion
<i>Chd.pl.</i> , choroid plexus	<i>G.g.co.</i> , conjoined (median) gasserian ganglion
<i>Ch.typ.</i> , chorda tympani nerve	<i>Gn.g.</i> , geniculate ganglion
<i>C.i.e.co.</i> , conjoined (median) capsules of internal ears	<i>G.s.p.</i> , great superficial petrosal nerve
<i>Cil.g.</i> , ciliary ganglion	<i>Gu.int.</i> , genu internum of the seventh nerve
<i>co.</i> , conjoined	<i>Hyp.</i> , hypophysis
<i>Co.rhmb.</i> , conjoined rhombencephala	
<i>Crp.str.</i> , corpus striatum	

- Ifd.*, infundibulum
II., nervus opticus
III., nervus oculomotorius
IIIr.fr., root fibers of third nerve
Infr., infraorbital nerve
Inf., infratrochlear nerve
I.o.m., inferior oblique muscle
IV., nervus trochlearis
IVr.fr., root fibers of fourth nerve
IX., nervus glossopharyngeus
Lat.r., lateral recess
Lat.v., lateral ventricle
Lg., lingual nerve
lt., left
Lyg.cg., laryngeal cartilages
m., muscle
Med.obl., medulla oblongata
Mdr.n., mandibular nerve
Mes., mesencephalon
Met.md., metencephalic mound
Met.co., conjoined metencephalon
M.i.g., median isolated ganglion
Mk.cg., Meckel's cartilage
Mk.cg.co., conjoined (median) Meckel's cartilages
ML., malleus
mo.nu.co., conjoined motor nucleus
m.r.fr., motor root fibers
Mr.ph., median raphé
Ms.m., masseter muscle
Mx.n., maxillary nerve
n.fs., nasal fossa
Nld., nasolacrimal duct
Ns., nasal (nasociliary) nerve
Nsp., nasopalatine nerve
nu., nucleus
Olf.b., olfactory bulb
Oph.n., ophthalmic nerve
Or.c., oral cavity
Ot.g., otic ganglion
Ped.fr., peduncular fibers
Pcot.cg., periotic cartilage
Pcot.cg.co., conjoined (median) periotic cartilages
Popt.r., preoptic recess
Pr.gl., parotid gland
R.c.nm., rostral cranial nerve-mass
r.fr., root fibers
rt., right
rhmb., rhombencephalon
S.l., sulcus limitans
S.lb., superior labial nerve
Slg.gl., sublingual gland
Smx.gl., submaxillary gland
S.o.m., superior oblique muscle
Sp.c., spinal cord
Sp.cn., spinal canal
Sp.g., spinal ganglion
Spl.g., sphenopalatine ganglion
Sp.n., spinal nerve
Sp.n.co., conjoined (median) spinal nerves
Sp.n.rd., spinal neural ridge
s.r.fr., sensory root fibers
S.r.m., superior rectus muscle
Stp., stapes
Stp.a., stapedial artery
T.A., tongue of head A
T.B., tongue of head B
Tm.smxl.gl.co., conjoined terminals of the median submaxillary and sublingual glands
Trach., trachea
Tr.sl., tractus solitarius
Tr.sl.co., conjoined (median) tracti solitarii
Tr.sp., tractus spinalis trigemini
Ts.sy., truncus sympatheticus
Ts.sy.ac., accessory truncus sympatheticus
Tl.md.obl., tip of tongue-like projection of the medulla oblongata
V., nervus trigeminus
Vb.a., vertebral artery
Vgg., conjoined (median) gasserian ganglion
VI., nervus abducens
VII., nervus facialis
VIIco., conjoined (median) VII nerve
VIII., nervus acusticus
Vm.r.fr., motor root fibers of V nerve
Vs.r.fr., sensory root fibers of V nerve
Vtr.III., third ventricle
Vtr.IV.co., conjoined fourth ventricles
Vtr.lat.quad., ventrolateral quadrant
Vx', uncertain branch of median V nerve
X., nervus vagus
XI., nervus accessorius
XII., nervus hypoglossus
Xm.nu.co., conjoined motor nuclei of median tenth nerves

DESCRIPTION OF THE NERVOUS SYSTEM

Spinal cord and spinal nerves

The gross anatomy is best shown by the model (figs. 4, 5, 6). The brain and spinal cord are well developed, larger than in a normal embryo of corresponding age, but not seemingly disproportionate to the size of the teratological embryo. They present no pathological or necrotic tissues or extrusions of brain substance such as are frequently found in abnormal embryos.

The spinal cord in the region studied gives off from the outer sides paired spinal nerves in normal manner and distribution. But along the median ventral surface of the cord there is a prominent neural ridge which diminishes gradually from about the level of the cervical flexure to the mediastinum. From this neural ridge there arise at regular intervals conjoined median spinal nerves which are unganglionated and unbranched (figs. 5, 20). Cross-sections of the upper cervical cord (figs. 18 to 20) indicate that the dorsal quadrants of the inner halves either do not exist or are very greatly reduced in this region, therefore the neural ridge consists chiefly of fused ventral quadrants of the juxtaposed members. The median spinal nerves seem to become successively smaller and to fade out after turning caudad in the midline for a greater or less distance. They finally disappear entirely and normal relations are maintained by spinal nerves of the outer (normal) sides.

Sympathetic nervous system

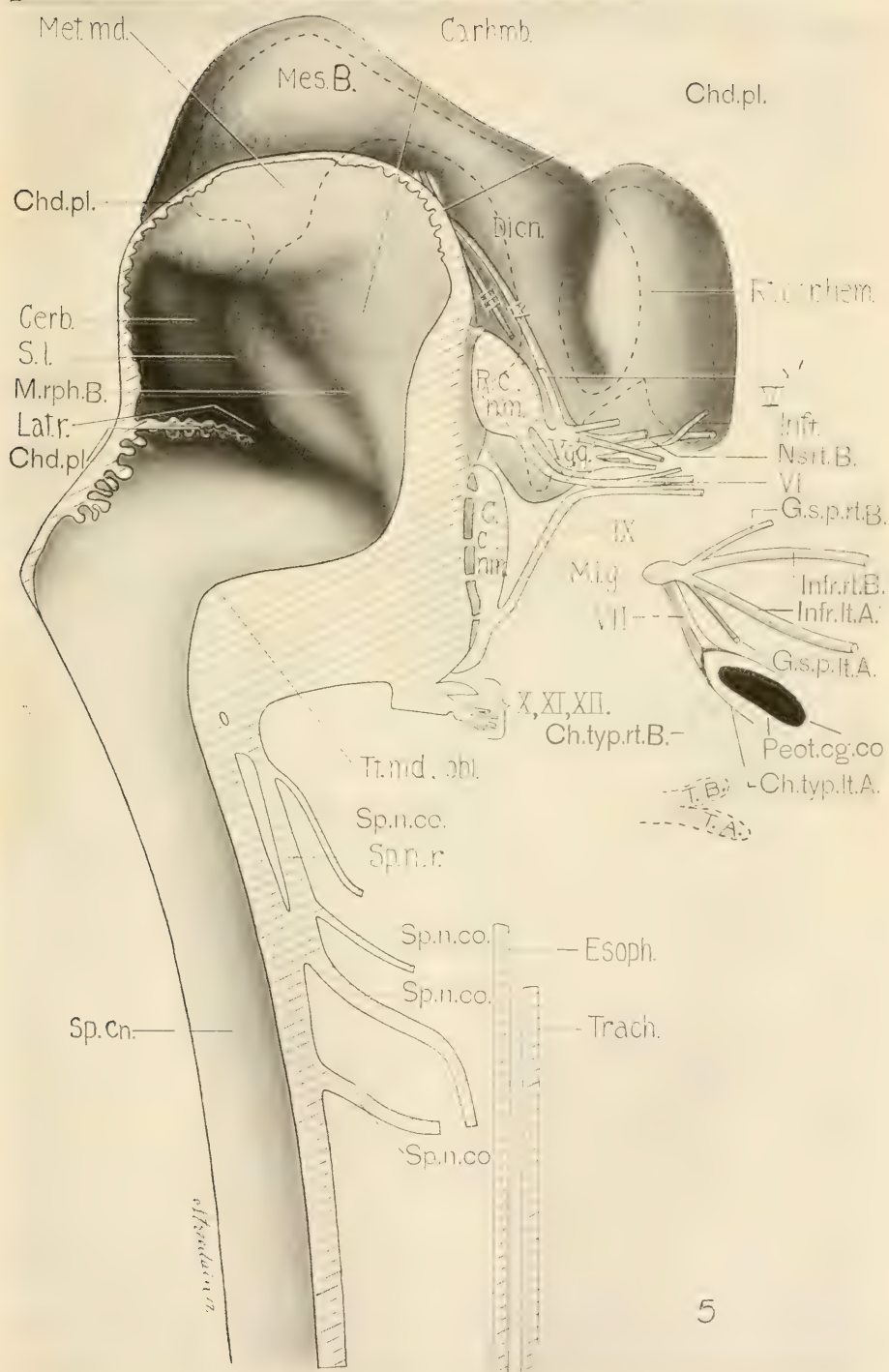
In the cervical region. In the neck region of each normal side a stout truncus sympatheticus lies parallel to the vagus nerve between it and the normal spinal nerves (fig. 7). The truncus curves dorsally around the ganglion nodosum and thus comes to lie between the vagus and the ventral surface of the spinal cord.

Fig. 4 External lateral view of the model of the brain and cerebrospinal nerves of head B (i.e., of its left or normal side). The tongue of head B, which lies in the median region, is added in diagram to show its innervation. The numbers upon the perpendicular at the right indicate the levels of the sections of the embryo represented in figures 8 to 20.

It then turns abruptly toward the midline and terminates in connective tissue medial to the ganglion petrosum of the ninth cranial nerve. In making this spiral turn around the vagus, it also crosses the glossopharyngeal and hypoglossal nerves dorsally. The model does not indicate a swelling of the sympathetic trunk in the region of the vagus ganglion, but it is undoubtedly the position of the superior cervical sympathetic ganglion. The course of the sympathetic trunk just described is perfectly normal, as figured by Streeter in Keibel-Mall ('12, part 2, fig. 103) and in figure 642 of Kollman's Handatlas ('07, part 2). In the teras, however, there is interpolated between this long ganglionic trunk and the normal spinal nerves a shorter sympathetic trunk extending from about the seventh spinal nerve caudad (fig. 7). This is in direct connection with the spinal nerves by typical rami communicantes on the one side and on the other with the long sympathetic trunk by shorter rami. How far below section 500 the sympathetic trunk extends I do not know, as these sections are not in my possession. After having reached the ventral surface of the bodies of the vertebrae, the lowest two of the median spinal nerves show a proliferation of cells at the distal end of the growing nerve trunk (fig. 20, s. 362). This presents a picture closely resembling the development of the spinal ganglia of the normal sides and is in harmony with the description given for normal development by Kohn ('07) in the rabbit, and Streeter in human embryos.

In the head. The otic, ciliary, sphenopalatine, and submaxillary ganglia in the outer (normal) half of each head are clearly demonstrable and conform to the descriptions given by Kuntz ('13). They may be readily identified in figures 15, 16, 17, 19. In the median region they are identifiable with much less certainty except the sphenopalatine ganglia. These are conspicu-

Fig. 5 Median sagittal section of the same model as figure 4. This shows the sculpturing of the inside wall of the conjoined rhombencephalon and the nerves of the median region. Cut surfaces are striated. The external surface view of the right side of the brain of head B is shown in perspective. The dotted line represents the ventricles of the diencephalon and forebrain projected upon the surface. Esophagus, trachea, tongues, and the conjoined periotic cartilages are added in diagram to show their relative relationships to the nervous system.



ously developed and easily recognized by their relationships to neighboring structures (figs. 13 to 15). The submaxillary ganglia are absent as are the lingual nerves with which they would be associated. In other words, the two tongues receive their lingual nerve supply from the outer (normal) sides only (fig. 19).

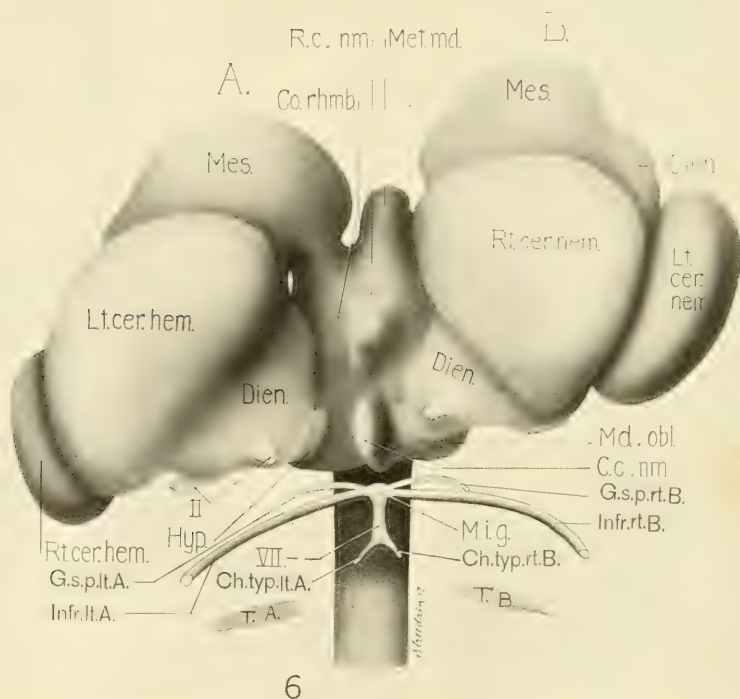


Fig. 6 Front view of the model of the teratological brain after removal of the nerves. The tongues are added in diagram to give their relative positions. The median isolated ganglion has no integral attachment to the brain, and therefore in the model is suspended by wires (not shown).

Presence of median ciliary ganglia is exceedingly doubtful. In sections 202 and 205 (not figured) there are in the location expected two or three small aggregations of cells that suggest ciliary ganglia, but are sufficiently uncertain to warrant caution. In close proximity to the median geniculate ganglion there is a dense aggregation of cells which may be conjoined otic ganglia.

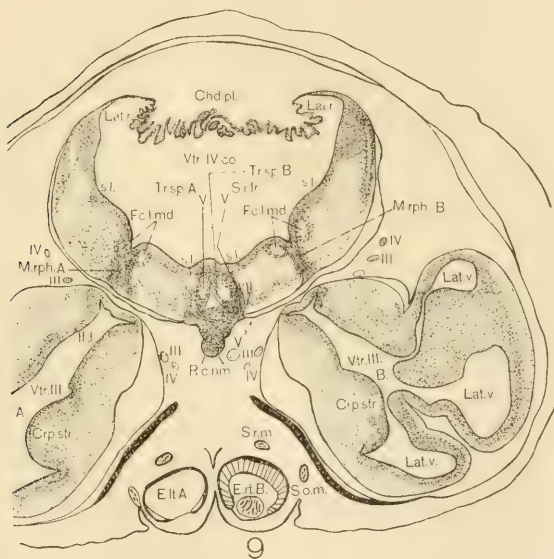
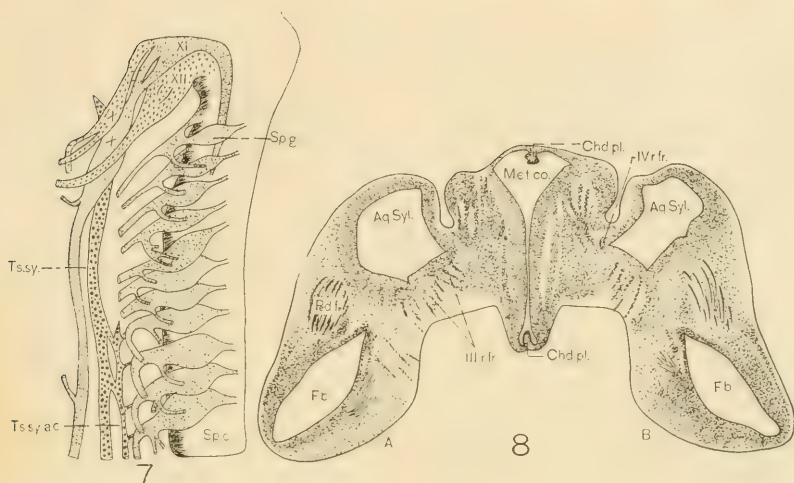


Fig. 7 Cervical sympathetic nervous system. A semi-diagrammatic drawing from the model showing the cervical sympathetic nervous system in relation to the neighboring cranial and spinal nerves.

Fig. 8 Section through the conjoined metencephalon (the 'metencephalic mound'). S. 96.

Fig. 9 Section through the conjoined fourth ventricle, the median eyes, and the forebrains of heads A and B. S. 163.

The brain

Simple observation of the brain model (fig. 6) shows certain conspicuous points of morphology, namely, that there is distinct bilateral symmetry; that each member of the teratological brain has a normal pair of cerebral hemispheres, a normal diencephalon and mesencephalon; that there is a broad space between the midbrains and a somewhat broader one between the forebrains of the two head members; that the normality and maximum development of the cranial flexures are so typical as to need no comment other than to call attention to them, and that interposed between the caudal ends of the mesencephala is the upper (rostral) margin of an enlarged region of the brain which, because of the sharp bend of the cephalic flexure of each head member, lies dorsal to the diencephala and hemispheres, but in reality is caudad to them and continuous with the spinal cord. This is obviously an enlarged rhombencephalon common to both members (i.e., conjoined) and therefore of special interest.

Briefly summarizing these structural points, it may be said that rostral to the cervical flexure the teratological brain shows increasing duplicity and divergence, the latter being greatest at the hemispheres, but in the process of doubling the primitive morphological relationships and the normal embryonic flexures have remained undisturbed.

A more critical study of the model and of the microscopical sections demonstrates the rhombencephalon to be considerably larger than normal, as would be expected, especially in its lateral dimensions, and to be associated with the principal abnormalities found in the head region of the embryo. The medulla is double, as indicated by a ventral forking of the central canal, which in cross-section has the appearance of an inverted Y (fig. 13). At the lower levels of the bulb the prongs of the Y are very shallow and gradually taper into a normal spinal canal. But rostrally the prongs flatten out and become obliterated as the medullary canal broadens into the spacious fourth ventricle (figs. 9 to 12). Between these two levels the brain tissue included between the prongs adjusts topographically to the space available. This is

clearly shown by comparing cross-sections at various levels; for example, at the lowest level it is somewhat evaginated, forming part of a cranial nerve-mass to be described later (figs. 16, 17), but at a somewhat higher level, and for about half the caudo-rostral thickness of the medulla, it is greatly narrowed laterally and elongated dorsoventrally, and owing to its limited space, projects tongue-like into the central canal, giving it the forked or inverted-Y appearance as described (fig. 13). At the rostral end, however, the medullary canal becomes incorporated into the fourth ventricle, and as the prongs of the Y flatten out in consequence thereof, the area between them narrows dorsoventrally and spreads laterally, thus contributing effectively to the abnormal width of the brain in this region and to the divergence of the two forebrains (figs. 6, 9 to 12). This lateral spreading is first noticeable at about the level of the superficial origin of the fifth pair of cranial nerves of the normal (outer) sides of the embryo. From here rostrally the angle of divergence increases steadily to the isthmi of the double brain. At this morphological level the rostral portion of the conjoined rhombencephalon (i.e., the metencephalon) abruptly narrows toward the median sagittal plane of the embryo, and forms a mound of tissue elongated dorsoventrally and lying between the separated caudal ends of the mesencephala (figs. 4, 6, 8).

A careful analysis of the brain tissue between the prongs of the Y-shaped canal shows it to be the walls of the juxtaposed sides of the two head members united in the median sagittal plane of the monster, i.e., a conjoined medulla made up of the fused dorsal and ventral quadrants of the left medullary moiety of head A and of the right medullary moiety of head B. The size and topography of these quadrants varies with the degree of fusion, as already indicated (seemingly a purely regulatory adjustment), but the interpretation of the area is, I believe, clarified by the identification of nervous elements within it and by other definite anatomical landmarks, such as the two sulci limitantes and the two median raphés of the conjoined halves of the two heads. The behavior of the quadrants in the mounded tissue between the midbrains is best understood after a description of the fourth ventricle, and is therefore deferred until then.

The outer walls of the conjoined hindbrains are of normal thickness and contain fiber tracts, nerve roots, and reception nuclei characteristic of a normal embryo. These are reserved for comment under their respective headings.

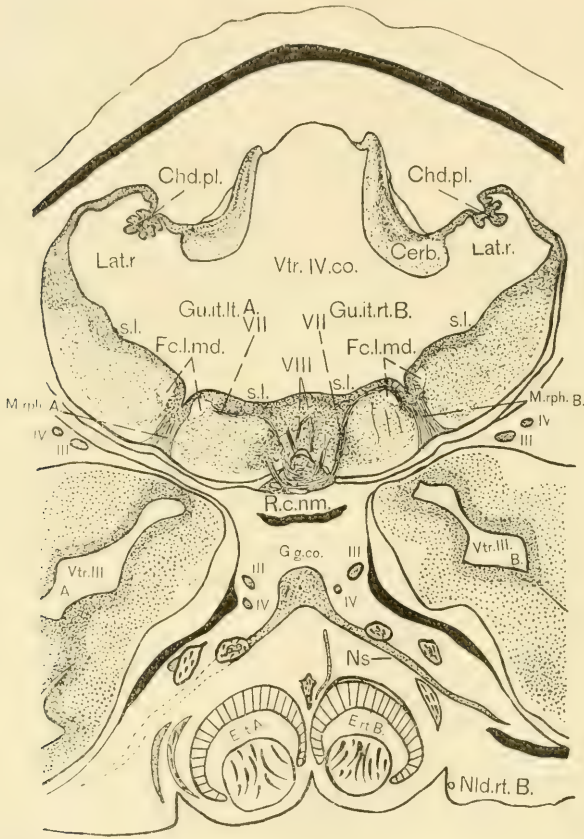


Fig. 10 Section through the cerebellum, motor roots of the median seventh nerves, the median gasserian ganglion (conjoined), and the median eyes. S. 188.

Cavity of the rhombencephalon. The fourth ventricles of the head members are confluent, but maintain the rhomboidal shape described for a single ventricle, although enlarged in proportion to the size of the teratological embryo. Lateral recesses are well developed on the normal sides of the ventricle, but there is

no indication of them in the conjoined region (fig. 10). The tegmen is of normal thickness. The choroid plexuses of the two heads are conspicuously developed, united in the middorsal line, and extend into the lateral recesses in normal manner (figs. 5, 9, 10). Any cross-section through the conjoined fourth ventricle will show distinctly a median raphé for each member, which marks the median sagittal plane of heads A and B, respec-

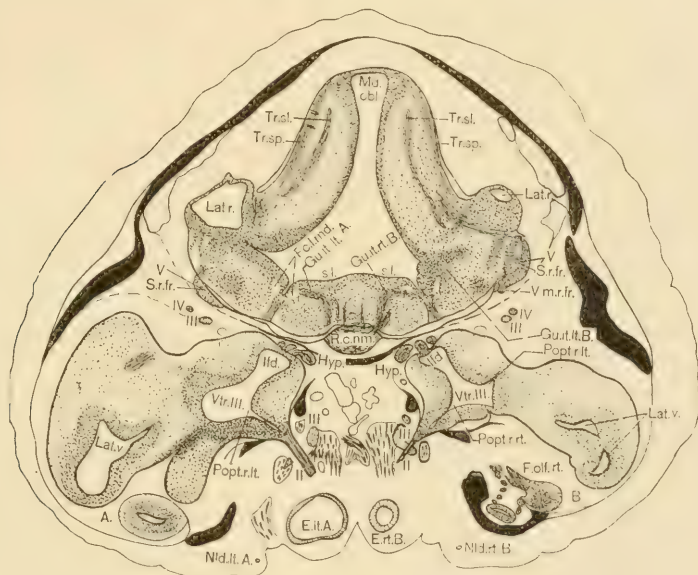


Fig. 11 Section through the superficial origin of the trigeminal nerves of the outer (normal) sides of the embryo, and the median optic nerves. S. 204.

tively, that is, the normal morphological axis of each head. At the outer side of each raphé is seen a distinct sulcus limitans dividing the walls of the rhombencephalon into dorsal and ventral quadrants (figs. 5, 9, 10) and in some of the sections the embryonic cerebellum may be seen bulging into the ventricular cavity from the dorsal quadrant of each normal side (figs. 5, 10). No cerebellar swelling is identifiable in the conjoined or median region.

It becomes necessary at this point to speak more fully of the median area of the brain (i.e., the area between the two raphés)

which, it will be remembered, began as compressed tissue between the prongs of the inverted-Y-shaped canal of the lower medulla, and by rostral spreading forms at the level under consideration the floor of the conjoined fourth ventricle. Both the sections and the model disclose partial doubling in this area, as demonstrated by a sulcus limitans medial to each raphé (figs. 5, 9, 10, 11). This ventricular floor consists, therefore, of two dorsal and two ventral quadrants, of which the latter become increasingly larger toward the isthmi and bulge into the ventricle, while the dorsal quadrants become correspondingly smaller and insignificant and are seen to lie in the median sagittal plane of the monster (figs. 9 to 15). More rostrally a cross-section through the embryo at about the level of the cephalic flexure shows that the dorsal quadrants have become so reduced that only a mid-dorsal choroid plexus remains, lying in the medial plane of the ventral surface of the teratological rhombencephalon. Still further forward this is seen to join the choroid plexus of the dorsal (normal) surface, thus forming a midline choroidal arch in the 'mound' between the mesencephala (figs. 5, 8).

It is obvious, then, that the left half of head A, instead of uniting with the right half of its own head, is joined to the right moiety of head B along the middorsal surface of the conjoined dorsal quadrants. This identification is important since it establishes three teratomorphological points, namely, the median sagittal plane of the monster, the line of fusion of the two heads, and the line of bilateral symmetry. Other evidence in support of the interpretation of the quadrants between the two raphés will be added when the central connections of the cranial nerves are discussed.

The gross anatomy of the mesencephala and telencephala may be dismissed with the brief statement that they give every appearance of normality, although in any given microscopic section there may seem to be asymmetry due, it will be remembered, to the downward tilting of head A with consequent obliquity in the plane of section.

Cranial nerves

Superficial origin and peripheral distribution of the nerves of the outer (normal) sides of the teratological head. As in the study of the brain, so in that of the cranial nerves, the region between members A and B is the area of greatest interest. But an accurate interpretation of the nerves in this median region requires first a careful study of the origin and distribution of those on the outer sides of the head where the picture conforms to normal conditions with striking exactness. Obviously, the investigation has necessitated the identification of many structures other than nerves that would serve as anatomical landmarks. Some of these have been labeled in the accompanying figures. Owing to the dearth of descriptive anatomy of normal embryos at the age of this teras, much of the interpretation has had to be made from gross anatomy of human adult and the descriptions of older embryos of a few of the lower mammals. Each interpretation has been rigorously checked by constant references to cross and longitudinal section series of normal pig embryos, especially those of 20, 22, and 25 mm. in length, and a few human ones.

The entire series of twelve pairs of nerves is present in normal linear arrangement, and each may be traced to such an extent as to leave no doubt of its identification. For convenience, the descriptions are given for the nerves of the left moiety of head B, the aspect shown in figure 4, but it should be remembered that they hold true also for the right moiety of head A, since normality is undisturbed in the outer half of each head member. For this reason the description of each nerve is very brief and given primarily for comparison with its mate in the median region. The central connections of the nerves are treated under a separate heading. The associated sympathetic ganglia have already been considered (p. 388).

I. *Nervus olfactorius.* The paired olfactory bulbs and primary olfactory nerves are normal for each head member. The fila olfactoria are readily identifiable in the cross-sections (figs. 11 to 14).

11. Nervus opticus. In considering this and the other ocular nerves, it should be mentioned that head A and head B, have a normal pair of eyes and eye muscles. Nasolacrimal ducts are demonstrable on each side of each head (figs. 10, 11, 13, 14, 16, 17, 18).

Tracing the left optic nerve of head B from the retina to the brain, it is seen to be surrounded by the origins of the muscles

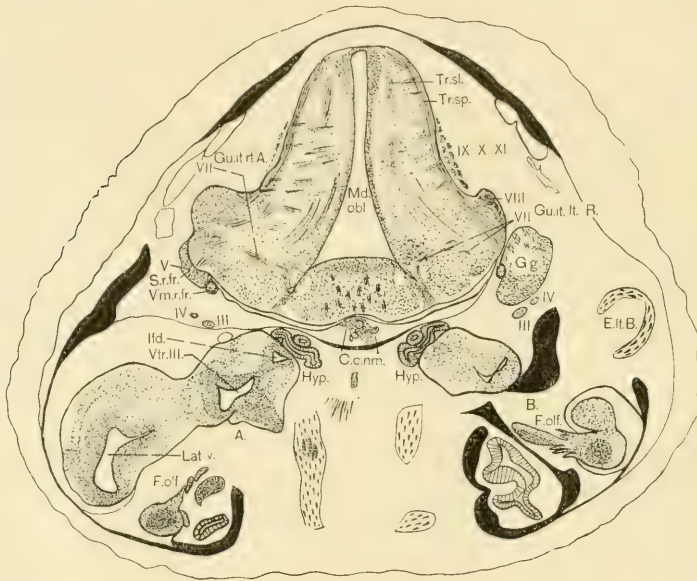


Fig. 12 Section through the motor roots of the seventh nerves of the outer (normal) sides of the embryo, the hypophyses, and the upper border of the nasal sacs. S. 214.

of the eyeball and to be accompanied by the ophthalmic artery on its outer and lower side. Near the eyeball it is penetrated by the central artery of the retina (fig. 15) and crossed by a branch of the trigeminus nerve above and by the oculomotor below. It converges toward the optic nerve of the opposite side (a nerve of the median region) to form a chiasma ridge rostral to the developing pituitary body and spinalward of the preoptic recess, which still opens into the cranial end of the

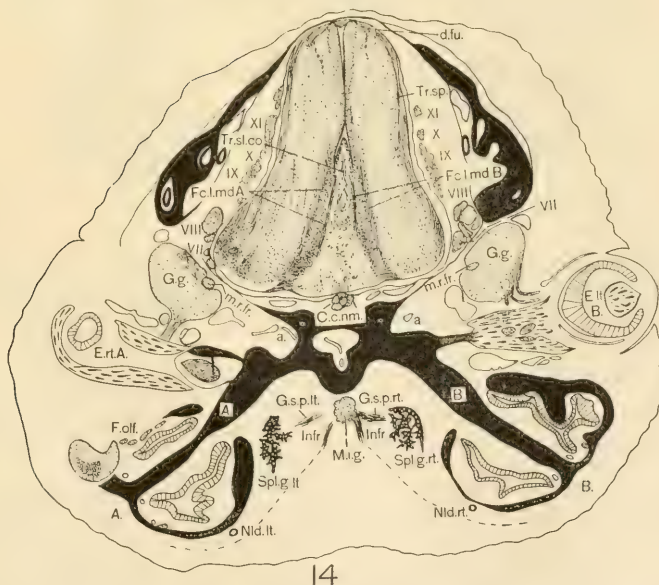
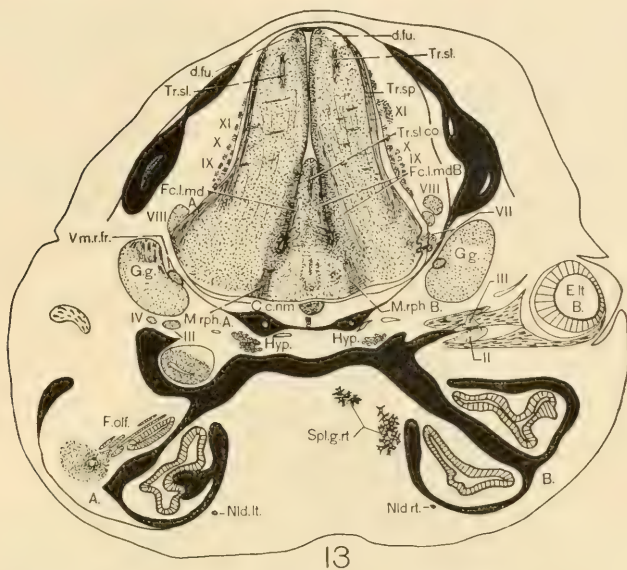


Fig. 13 Section through the gasserian ganglia of the outer (normal) sides of the embryo, and the upper border of the left (outer) eye of head B. S. 228.

Fig. 14 Section through the median isolated ganglion (conjoined geniculate), and the median sphenopalatine ganglia. The course of the infra-orbital nerves has been added in dashed lines. S. 234.

optic nerve (fig. 11). I was unable to trace fibers across the chiasma ridge, and as yet the external optic chiasma of adult brain is undeveloped.

III. Nervus oculomotorius. From its superficial origin at the concavity of the cephalic flexure the third nerve pursues a ventral and slightly rostral course medial to the fourth nerve, and at the level of the eye turns outward to supply the superior,

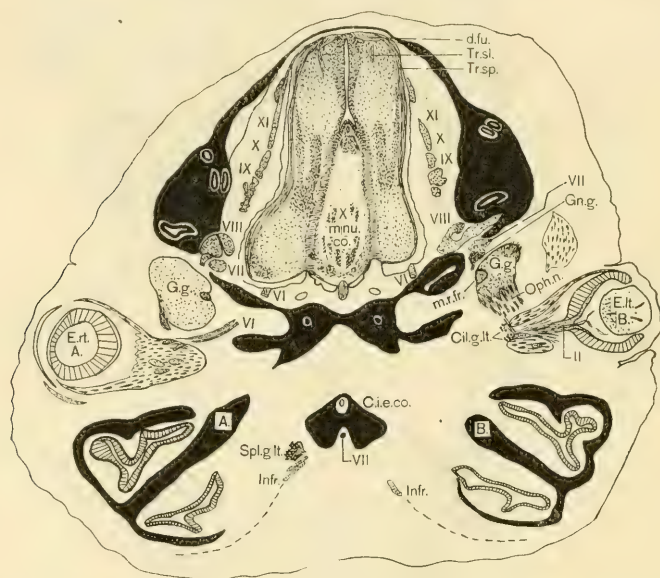


Fig. 15 Section through the two outer (normal) eyes of the embryo, and the median (conjoined) internal ear capsules. The ciliary ganglion of the left side of head B has been added from section 243. S. 242.

inferior, and medial recti muscles, and the inferior oblique. The superior palpebral branch is absent, as would be expected from the absence of the superior palpebral muscle.

IV. Nervus trochlearis. Spinalward of the oculomotor, the trochlearis emerges from the dorsal surface of the brain at the isthmus, swings around the cerebral peduncle, and courses external to the third nerve in a ventro-rostral direction to its termination in the superior oblique muscle of the eye.

V. *Nervus trigeminus*. The fifth nerve arises in typical normal manner by a large sensory and a small motor root from the ventrolateral surface of the pons, just at the pontine flexure. Immediately outside of the dura mater the sensory root expands into the large gasserian ganglion, which gives rise to the ophthalmic, maxillary, and mandibular divisions characteristic of the fifth nerve (fig. 4). Not all of the secondary branches of these

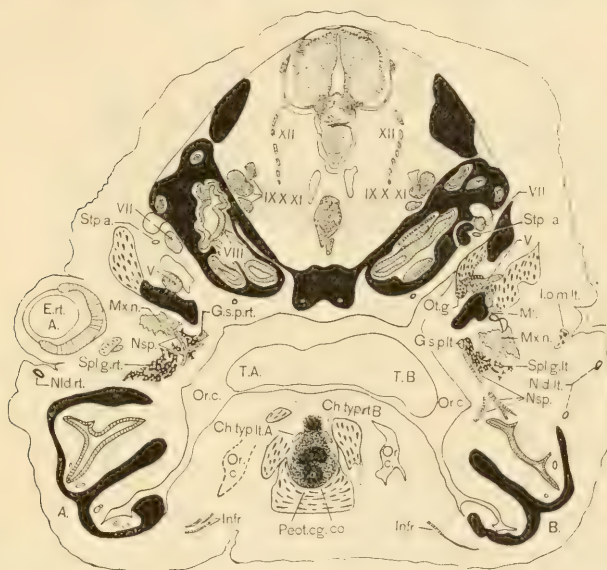


Fig. 16 Section through the internal ear labyrinth of the outer (normal) sides of the embryo, the sphenopalatine ganglia of the outer sides, and the median (conjoined) periotic cartilages. S. 262.

are as yet developed, and only those that have definite relation to the median region are labeled in the figures.

Almost from its beginning the motor root is embedded in the gasserian ganglion, and ultimately becomes merged with the mandibular branch (figs. 13 to 15).

The ophthalmic division courses rostralward over the optic nerve and beneath the trochlear, and divides into normal terminal branches. The nasal and infratrochlear branches are readily traced to their terminations.

The maxillary division arises from the middle of the ventral surface of the ganglion and follows a normal distribution. Figures 16 and 17 show its course through the developing sphenopalatine ganglion (left) and on into the mucous membrane of the nose by way of its nasopalatine branches. The continuation

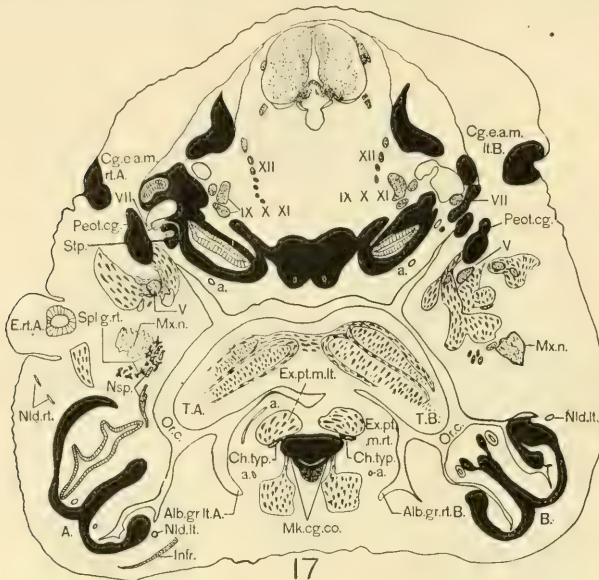


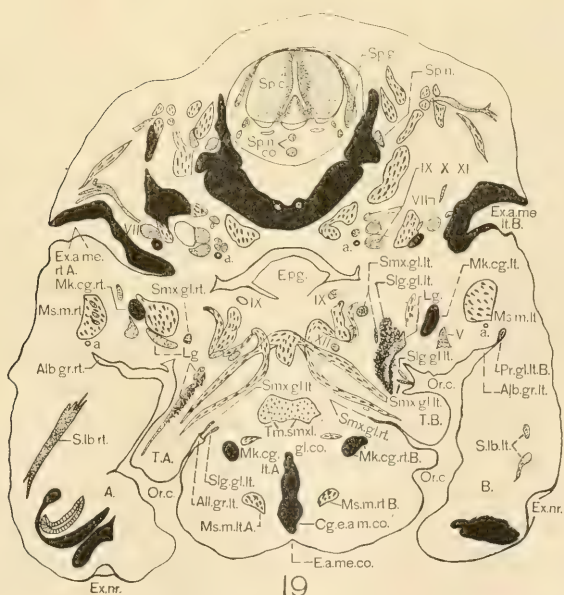
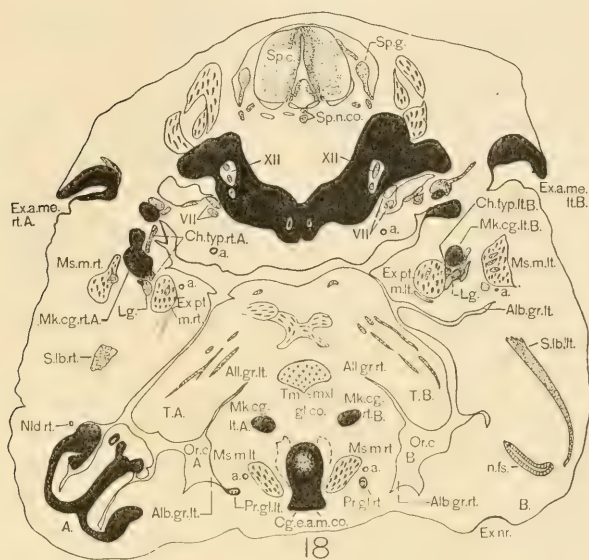
Fig. 17 Section through the cartilages of the external auditory meatuses of the outer (normal) sides of the embryo, the two tongues, and the median Meckel's cartilages at their fused otic ends. S. 272.

Fig. 18 Section through the hypoglossal foramina, the external auditory meatuses of the outer (normal) sides of the embryo, the tongues, and the conjoined cartilages of the external auditory meatuses of the median region. S. 286.

Fig. 19 Section through the roots of the first spinal nerves, the epiglottis, and the median (conjoined) external auditory meatus. S. 302.

of the main trunk and the superior labial branches are also seen in figures 17, 18, 19.

As already stated, the motor root of the trigeminus is merged with the mandibular nerve, the sensory portion of which arises from the most ventral region of the gasserian ganglion. The common trunk courses rostrally, and soon divides into its terminal branches, of which only the lingual concerns the present investi-



gation. The auriculotemporal and inferior alveolar branches are identifiable, however.

The lingual branch is of special interest, because in this teras there are two tongues united at their roots, but innervated only from the outer (normal) sides of the two heads (figs. 4, 19). Whether or not these nerves would have given sufficient innervation for normal functioning of the tongues had the teras developed to term is impossible to say. The chorda tympani branch of the seventh nerve, which accompanies the lingual nerve from the external pterygoid muscle to the tongue, is well developed (fig. 18).

VI. Nervus abducens. The superficial origin of the abducens is medial and slightly caudal to that of the fifth nerve. It curves outward around the ventral border of the gasserian ganglion, coursing between the ganglion and the internal carotid artery, the third and fourth nerves. It terminates in the external rectus muscle of the eye (figs. 4, 15).

VII and VIII. Nervi facialis and acusticus. Embryologically, these two nerves are so closely associated it is convenient to consider them under one heading. The seventh nerve is readily recognized by the geniculate ganglion on its sensory root, which lies in normal embryonic relation to the auditory capsule and the sensory ganglion of the trigeminus (fig. 15). From its ganglion the facial nerve gives off peripherally the posterior auricular, the mandibular, the inferior alveolar, the superficial petrosal, and the chorda tympani branches—all easily identified by their distribution. Traced brainward from the geniculate ganglion, the nerve is followed with equal ease through the facial canal and is seen to come into normal relation with the eighth nerve (figs. 13, 14, 15). Near the ganglion the nervus intermedius of Wrisberg is recognized lying between the motor root of the seventh and the acoustic ganglion, but a little farther cranial it seems to be lost among the fascicles of the eighth nerve. The motor root of the facial nerve emerges from the ventrolateral margin of the medulla, ventrocaudad of the roots of the trigeminus, and ventromedial of the acoustic, i.e., between the fifth and the eighth nerves (fig. 4).

The eighth nerve. The vestibular and cochlear contributions to the conspicuous ganglion acusticum are readily identified. Their roots enter the brain in small root bundles composed of several fascicles and more or less distinguishable one from the other. The common entrance is at the lower border of the medulla, caudolateral to the facial, and overhung by the lateral recess of the fourth ventricle (figs. 4, 12).

IX, X, and XI. Glossopharyngeus, vagus, and accessorius. These three nerves are also grouped together because of the intimate relationship that exists at their superficial origins. The accessorius arises by a series of small bundles in the region of the cervical spinal nerves, and mingles with similar rootlets of the vagus as the latter emerges along the outer surface of the medulla (figs. 4, 13 to 17). Beyond the ganglion nodosum of the vagus I was not able to trace the independent course of the accessorius continuously, but some of its peripheral fibers were identifiable among the muscle masses of the shoulder.

The glossopharyngeus is recognized at its superficial origin as a large bundle of rootlets at the rostral end of the vagus series.

The peripheral distribution of the ninth and tenth nerves is easily followed (figs. 4, 7). The vagus courses along the neck in typical normal manner, giving off a well-defined auricular branch which receives an anastomosis from the seventh, a recurrent laryngeal, and cardiac branches. The ganglion nodosum is very large.

The ninth nerve runs parallel to the tenth, at first medial, then rostral, then medial again, and is lost in the region of the larynx and common root of the tongues.

XII. Nervus hypoglossus. The twelfth nerve arises by several rootlets in linear series with the ventral roots of the cervical spinal nerves, and therefore medial to the 9-10-11 series (figs. 4, 16, 17, 18). Soon after piercing the cranium these rootlets unite in a common trunk which twists in a semispiral around the ganglion nodosum to its outer border, and at its caudal extremity turns abruptly rostralward to its termination in the tongue of head B.

Superficial origin and peripheral distribution of the nerves of the median (conjoined) region. The relationship of structures in this region, due to the juxtaposition of the head moieties, should not be forgotten. The identification of at least a few structural landmarks is an essential guide to nerve identification, and these are specially considered in relation to nerve VII.

In dealing with teratology from a very different viewpoint, Wilder ('08) discussed the nerves concerned with the musculature of the median eyes of this embryo (Teras I) and hazarded an interpretation of some others. His investigation in the latter regard was admittedly less detailed than the present study, and while agreeing with many of his findings, others are amplified, and still others are at variance, as may be noted by a comparison of the following description with that of Wilder ('08 pp. 412-417, fig. 29).

The present study of the median region has been made by careful comparison with known structures in the outer (normal) moiety of each head, both regions again rechecked by normal embryos, and the cartilages further verified by a wax-plate model of the chondrocranium of the teras and of a normal embryo slightly older.

Nerves one, two, three, and four are independent of fusion or doubling and may be dismissed without further comment, since they are merely normal mates of those on the outer side of each head, respectively. The real problem begins, therefore, with the trigeminus and involves all of the cranial nerves caudad to it. Figure 5 represents a median sagittal section through the model and shows with considerable clearness the relationship of the median nerves to each other and to the brain.

Earlier in the paper it was pointed out that there is a neural ridge along the median ventral surface of the spinal cord, which gives rise to median (conjoined) spinal nerves. Attention is now called to two median cranial ridge-like masses along the ventral surface of the medulla, which are separated from each other and from the spinal ridge by a short hiatus (figs. 6, 5). These cranial ridge-like masses are not evaginations of the brain wall, as the spinal ridge is an evagination of the spinal cord,

but rather, masses of tangled nerve fibers and cells of uncertain significance, attached to the brain wall by short strands of nerve fibers (figs. 5, 9 to 12). In contrast, therefore, these are designated cranial nerve-masses which are spatially separated into two morphologically distinct aggregations, the one almond shaped and rostral to the other which is a longitudinally elongated mass. The former is designated as the rostral cranial nerve-mass (figs. 5, 6, 9, 10, 11), the latter as the caudal cranial nerve-mass (figs. 5, 6, 12 to 14). Each receives a definite set of nerve roots. The topographical position of these two cranial nerve-masses gives a clue that is confirmed by tracing the median nerves brainward from their peripheral distributions, in so far as this is possible. It should be mentioned in passing that there are fiber strands scattered through this median region with no peripheral or proximal connections and therefore impossible of accurate identification. By the brainward tracing of the identifiable nerves, the rostral cranial nerve-mass is apparently a 5-6-7-8 nerve complex, and the other a 9-10-11-12 complex (fig. 5).

A median (conjoined) gasserian ganglion is a conspicuous neurological landmark of certain identification in the fused area of the two heads (figs. 5, 10). It is small as compared with the gasserian of either normal side, but large for the limited space of the median area. From it an ophthalmic division with a conspicuous nasociliary branch is given off to the inner side of each head. Other small branches are also given off, but lose themselves in near-by tissue without yielding assurance of identity. The ganglion connects with the rostral cranial nerve-mass by a median compact strand of fibers which could not be traced through it with certainty (fig. 5). To one side of the rostral cranial nerve-mass, and lying between it and nerves three and four of the right (inner) side of head B, a short, stout branch from the ganglion ends abruptly in connective tissue and its identification is therefore vague (fig. 5, 9).

Above the ganglion there is a pair of detached, unidentifiable nerves on either side of the midline, which may well belong to the median trigeminus, since the fifth nerve has such an extensive distribution, but again there is no assurance of accurate identity.

Nerve VI. The median abducens lies in the median plane below the conjoined gasserian ganglion, and enters the same cranial nerve-mass dorsal to the fifth nerve (fig. 5). It is identified by its distal branches which innerve the external recti muscles of the median eyes and a portion of the retractor bulbi. At just this region the interpretation of the sections is exceedingly difficult for the nerve fibers all seem to stream together beneath the gasserian ganglion and become obscured by it. Therefore a separate model of this area was made.

Nerve VII. Of the two median facial nerves, each has been identified with certainty from its genu internum to the rostral cranial nerve-mass, but I was not able to trace the fibers through the mass (see Central connections of the cranial nerves and the associated fiber tracts). The peripheral fibers are directly related to the median isolated ganglion and are considered in connection with it.

Nerve VIII. No peripheral fibers of median acoustic nerves were identifiable, although conjoined cartilage of the median internal ear capsules is present.

Nerve IX. Immediately below the abducens and parallel with it in the median line there is another nerve of almost twin appearance, which however, emerges from the caudal cranial nerve-mass (fig. 5). It may be a median ninth, but again certain identification is not possible, since its peripheral distribution is indefinite.

Ventral to these abruptly terminated nerves there are still other fine, detached fibers scattered through the tissue on either side of the midline, some indicating a course to the juxtaposed external surfaces of the head members, i.e., toward the median line of the monster. The identification of these branches is little more than guesswork, however, for neither cranial nor peripheral connections were seen.

Nerves X, XI, and XII. Just caudal to the uncertain ninth nerve, a shorter one arises, probably the vagus (fig. 5). Behind this one, short stumpy roots emerge from the nerve-mass, but end abruptly in near-by tissue. They suggest the remaining median cranial nerves, accessorius and hypoglossus. This

caudal cranial nerve-mass is separated by a short hiatus from the rostral end of the median spinals (fig. 5).

The median isolated ganglion

Wilder ('08, p. 419) speaks of this ganglion as follows: "Posterior to this" (i.e., a long ganglionic ridge extending longitudinally in the midventral line posterior to the sixth nerve) "and still in the median line are two farther nerves which may be regarded as cranial, the first smaller and the second large" (the probable ninth and tenth). "About opposite these ventrally lies a large median ganglion, entirely detached from them and from the cord, yet from this proceed two pairs of nerves, the anterior ones very fine and short, the posterior ones larger and longer. These nerves seem soon to lose themselves in the surrounding tissues." He then identifies a glossopharyngeal and vagus, and adds: "The detached ganglion is less certain" (than the probable 9th and 10th) "at least until after a careful determination of the rudimentary structures to which its nerves are distributed, but it is probably either the ganglion petrosum of the ninth or the ganglion nodosum of the tenth, or possibly both together."

From the evidence at hand I feel obliged to disagree with Doctor Wilder's interpretation, although the ganglion lies in the plane of the median 'vagus complex' (the caudal cranial nerve-mass of this paper). The anatomical factors that support the difference of opinion are the identifications of certain structural landmarks in this median region, which has been referred to several times as a region of special interest. Until these were identified the ganglion remained the neurological conundrum of the embryo. It seems advisable, therefore, to digress long enough to establish these landmarks before hazarding an interpretation of the ganglion. The several reconstruction models were invaluable in this connection.

The only external landmark to be noted is a slight depression in the midline of the teras below the median eyes and between the inner angles of the mouths. This is a median (conjoined) external auditory meatus (figs. 1, 2, 19). Studying first in the sections the normal (outer) sides of heads A and B, the junction

of chorda tympani and lingual nerves identified the external pterygoid muscles (fig. 18). The developing parotid glands, and therefore the masseter muscles, the submaxillary and sublingual glands were identified (figs. 18, 19). These were then readily found on the inner side of each head member. Here the masseter, external pterygoid muscles, and parotid glands are quite independent for each head (figs. 18, 19), but the submaxillary and sublingual glands terminate in a conjoined condensation of connective tissue (figs. 18, 19).

Moreover, by tracing Meckel's cartilage on the normal side of head A and head B from symphysis mentis to its proximal termination, the malleus, there is established another definite landmark. Meckel's cartilages of the median region (i.e., the left one of head A and the right one of head B) were then traced craniad in similar manner and were found to converge and fuse in the midline at about the level of the common root of the two tongues, thus forming conjoined Meckel's cartilages at or near their otic ends (fig. 17). The model of the chondrocranium (not figured) shows a thickened knob of cartilage at this point which undoubtedly represents united periotic cartilages. The sections show this cartilage extending through several millimeters surrounded by diffuse connective tissue and more or less undifferentiated muscle masses (fig. 16).

Lying in the midline of the monster between this conjoined periotic mass and the median external auditory meatus is an elongated strand of cartilage which topographically identifies it as conjoined cartilage around these fused external meatuses (figs. 18, 19). This interpretation is further supported by the relationship of the cartilage to the parotid glands and masseter muscles which flank it on either side, remembering that the midline of the monster represents juxtaposed external surfaces of the two heads. The glands and muscles are then in normal morphological relationship to the conjoined external auditory meatal cartilages and the oral cavity of each head.

A mass of cartilage representing united internal ear capsules of the conjoined heads, and probably involving the sphenoids, too, lies between the fused periotic cartilages and basis cranii

(also fused). This appears in section 242 (fig. 15) as a winged mass equidistant from the basis cranii and nasal septa of the two snouts. It is shown in relation to the basis cranii in section 232 (fig. 14).

Two other important landmarks have already been mentioned. These are the sphenopalatine ganglia of the median region, not fused, but independent for each moiety of its respective head (figs. 13, 14, 15).

In summary, the following anatomical landmarks have been established in the median region between the two snouts, external to the brain: 1) non-conjoined or independent structures—parotid glands, developing ducts of submaxillary and sublingual glands, masseter and external pterygoid muscles, sphenopalatine ganglia; 2) conjoined structures (i.e., contributions from the left half of head A and the right half of head B)—a submaxillary and sublingual terminus, Meckel's cartilage (otic ends), cartilage of the external auditory meatuses, periotic cartilage of the middle ears, cartilagenous capsule of the internal ears. All are considerably reduced in size, as might be expected from the limited space into which they have been cramped.

With these landmarks in mind, the identity of the median isolated ganglion may be satisfactorily established. The ganglion itself is slightly flattened and lies close to, but not touching, the conjoined internal ear capsules. If the "two pairs of nerves that proceed from its lateral borders" be traced peripherally they are seen not to "lose themselves in the surrounding tissues," but to pursue a definite, recognizable course. The 'anterior ones' lead directly into the sphenopalatine ganglia of the median region; the 'posterior ones' course rostrally around the cartilages of the nasal capsule of each snout to the upper lip (figs. 14 to 16). In addition there emerge from the under surface of the ganglion two slender nerve strands which descend parallel to each other for a very short distance, then separate, sending a branch to either side of the median periotic cartilage, and somewhat rostral to the fused otic ends of Meckel's cartilages each turns beneath the external pterygoid muscle toward the oral cavity of its respective head (figs. 15 to 17). All the morpho-

logical and topographical evidence, when checked by comparison with the normal sides of the teratological head, identifies the median isolated ganglion as a conjoined geniculate ganglion, the 'anterior' pair of nerves as great superficial petrosals, the 'posterior' pair as infraorbital branches of the VIIth nerve, and the pair that take origin from the under side of the ganglion as median chorda tympani, although, as stated earlier in the paper, no median lingual nerves seem to be present.

If these interpretations are correct, they establish morphological symmetry of parts for each head, although topographically the organs lying nearest the external surface of each head have been considerably cramped and somewhat reduced in size, and the more dorsal structures have been the most dislodged from their normal position in this mandibulomaxillary complex. The striking fact lies not in these regulatory, topographical adjustments, it seems to me, but in the tenacious dominance of the normal morphological relationships.

Wilder ('08) was right in interpreting the isolated ganglion as a member of the cerebrospinal system, rather than of the sympathetic, but the anatomical evidence identifies it with the seventh nerve, not with the ninth or tenth, as he thought.

Central connections of the cranial nerves and the associated fiber tracts

In the normal regions of the teratological head. The course of the nerve fibers within the brain is exceedingly difficult to follow because they are non-medullated and are not stained with a specific stain. The following account is therefore more or less fragmentary.

No special word concerning the olfactory and optic nerves need be added here.

III. The oculomotor nerves arise in typical manner from ventral neuroblasts of the mantle layer of the mesencephalon. They give rise to fiber strands that converge into rootlets which emerge in a common trunk from the concavity of the cephalic flexure. Neither the nucleus nor decussating fibers were identifiable (fig. 8).

IV. The intracranial fibers of the fourth nerve are obscured by the dense cells of the mantle layer, and I was unable to trace their decussation (fig. 8).

V. Within the marginal zone of the medulla on each normal side the sensory root fibers of the trigeminus form a flat longitudinal tract just beneath the surface, which descends as a typical tractus spinalis of the fifth nerve (figs. 11 to 15). Neither the motor nucleus nor the mesencephalic root fibers could be identified with certainty.

VI. The intracerebral course of the abducens fibers was not traceable.

VII. The motor fibers of the facial nerve from the surface of the brain across the pons, beneath the floor of the fourth ventricle to the genu internum, were readily followed, but from here to their nucleus of origin it was not possible to trace them with certainty (figs. 11, 12). The fibers of the nervus intermedius, or sensory seventh, penetrate the brain in very close relation to the eighth nerve, but I did not succeed in tracing them with certainty across the tractus spinalis of the fifth nerve into the tractus solitarius, which is conspicuous in sections of the medulla (figs. 11, 12, 13).

VIII. The course of the acoustic fibers within the brain was equally indefinite.

IX and X. The intracerebral connections of these nerves are intimately associated with the tractus solitarius. Afferent ganglionic fibers from both nerves penetrate the brain by a series of rootlets along the lateral wall of the medulla and pierce the mantle and marginal layers almost at right angles, some of the fibers to enter the tractus solitarius, others their terminal nuclei, which lie between the solitarius and the central canal (figs. 12, 13).

XI. Filaments of the spinal accessory arise from cells in the anterior column of gray in the upper cervical segments of the spinal cord and emerge from the lateral surface of the cord and medulla as the spinal root of the accessorius.

XII. The fibers of the hypoglossus were not traceable from the surface of the brain to their nucleus of origin.

The dorsal, lateral, and ventral funiculi of the spinal cord and medulla on the outer (normal) portions are clearly demonstrable (figs. 13 to 19).

Before leaving the normal area, however, there are certain other fiber tracts that should be considered: A longitudinal fiber tract, the fasciculus longitudinalis medialis, may be traced along each side of the median raphé of each head rostrally from about the level of the superficial origin of the normal seventh nerves to and extending throughout the entire extent of the medulla and mesencephalon (figs. 9 to 14). The fibers of the basal portion of the cerebral peduncle, or ventral part of the mesencephalon of each head, are conspicuous as they sweep upward from the medulla and arch over the cephalic flexure on their way into the diencephalon and hemispheres (fig. 8). Dorsally they form the tegmentum, which constitutes the side walls and floor of the aqueduct of Sylvius.

Fibers of the posterior commissure are seen only in oblique section, but the commissure is normal.

In the conjoined regions. In the median region the central connections of the cranial nerves are still more problematic, for they involve tracing the peripheral fibers through the two cranial nerve-masses into and through regions of the brain that are distinctly teratological in form relations and size that adjust topographically to the space available. The alterations of the normal relationships of the quadrants in this median region from the cord to the mesencephalon must ever be kept clearly in mind if the normal pattern of the intracranial nerve fibers and fiber tracts is to be recognized through the teratological relationships.

Nerves one, two, three and four are not involved in the problem.

The rostral cranial nerve-mass, its associated nerves and fiber tracts

At the level of the entrance of the median fifth nerve into the rostral cranial nerve-mass, it is seen that juxtaposed dorsolateral and ventrolateral quadrants form the median area, and the

midline itself is therefore the line of union between the external (peripheral) surfaces of the dorsal quadrants (fig. 9). On either side of the midline, but very close to it, is a fiber tract, which by analogy with the tracts in similar position on the normal sides of the teratological head is believed to be a spinal fifth tract of the left and right sides of the two heads, respectively (fig. 9). In size each tract is greatly reduced, proportionate to the reduced size of the quadrants, but in extent quite in keeping with the elongated, normal *tractus spinalis*. In shape it conforms to the changing configuration of the quadrants, and rather far rostrally it curves crescentwise into the ventral quadrant, which, however, lies lateral to the dorsal quadrant.

Bundles of nerve fibers from the cranial nerve-mass cross the ventral end of the median spinal fifth tract and turn spinalward at a sharp angle to keep within the dorsal quadrant, as it were, only to lose themselves in the dense cells of the mantle layer. These lie laterodorsal to the spinal fifth tract, but represent a median position in normal morphology. They suggest sensory fibers of the fifth nerve (fig. 9). Other fibers cross the ventral end of the tract and take a more lateral direction toward the ventral quadrant, but since the line of demarcation between the two quadrants is an arbitrary one drawn from the *sulcus limitans* to the periphery, it is exceedingly difficult to determine just where the fibers end, since they are obscured by the cells of the mantle layer. Although some of them may be motor fibers of the fifth nerve, I believe most of them to be sensory fibers of the trigeminus, for this is the chief nerve involved at this level.

VI. Nothing definite could be established for the median abducens fibers.

VII. The intracerebral course of the median pair of facials is distinctly traceable from the *genu internum* to the cranial nerve-mass, but here they interlace in such manner as to render further identification impossible (figs. 10, 11).

VIII. From the caudal area of this rostral cranial nerve-mass, but teratologically medial to the seventh nerves (i.e., normally dorsal), a bundle of nerve fibers enters the brain on either side of the midline of the monster and is faintly traceable in the

mantle layer of the conjoined dorsal quadrants (figs. 10, 11). By analogy with the normal topographical relations of the V-VII-VIII group of nerves, they suggest median acoustic fibers.

The caudal cranial nerve-mass, its associated nerves and fiber tracts

IX, X, XI, XII. There is little to be said that is definite concerning the nerve roots of the caudal cranial nerve mass. Approximately the lower half of this mass is in fiber connection with that portion of the median medulla which extends tongue-like into the medullary canal. By this invagination it will be recalled from the description of the gross anatomy of the brain that the conjoined dorsolateral quadrants are toward the tip of the 'tongue,' and are therefore narrow and tapering, while the ventrolateral quadrants are broader and lie immediately ventral. Into this distorted topography of the quadrants bundles of fibers enter from the tangle of the nerve-mass only to become tangled again in a confusion equally hopeless of clarification (figs. 12, 13). However, by analogy meager understanding is possible.

Attention has already been directed to the fasciculus longitudinalis medialis on either side of the median raphé of each head moiety (figs. 9 to 12). More caudally fibers of these fasciculi may be followed dorsally along the sides of the forked central canal of the medulla, i.e., into the median attenuated dorsal quadrants (figs. 13, 14). Other fibers are seen to converge toward the midline, or to merely tangle up within the median area (figs. 13, 14). In the midline of the fused dorsal quadrants there is a sharply defined fiber tract which is probably a conjoined tractus solitarius (figs. 13, 14), and in the fused ventral quadrants there is a rounded aggregation of cells and interlaced nerve fibers that strongly suggests the motor nucleus of the vagus complex (fig. 15). All intertangled among these fiber tracts and embryonic cells are the root fibers of the cranial nerves of the caudal cranial nerve-mass.

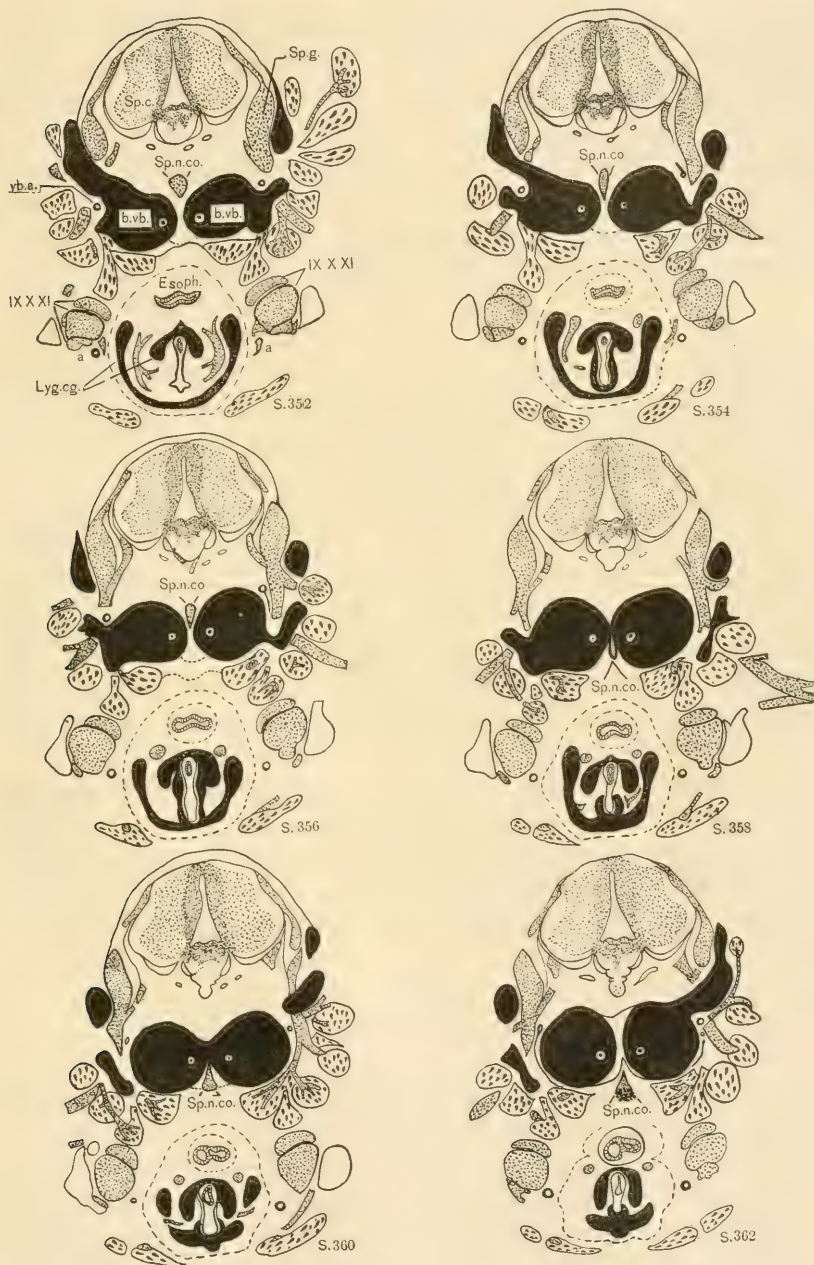


Fig. 20 Six alternate sections showing the relation of the median (conjoined) spinal nerves to the spinal cord, the normal spinal nerves, and the bodies of the vertebrae. S. 352-362.

Some of the above interpretations of intercranial fibers of the median region may seem too speculative, but with a knowledge of the normal segregation of nerve fibers into dorsal and ventral quadrants, and recognizing the spatial separation of the two cranial nerve-masses plus the certain identification of some of the nerve components in each, by elimination and analogy the speculations on the remaining median nerves and their associated fiber tracts are after all rather closely guarded.

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The study of the nervous system has been made under the guidance of Prof. C. Judson Herrick, of the anatomical department of the University of Chicago. To him I feel especially indebted, for his kindly attitude has been a constant stimulus to further research and his assistance in neurology of inestimable value.

SUMMARY

A detailed study has been made of the nervous system in a laterally symmetrical dicephalous pig embryo 22 mm. in length, and the following data determined:

1. The foreparts of the two head members diverge from the median sagittal plane at the same angle, but the right member (A) is tilted downward somewhat more than the left member (B) and the whole head is twisted slightly to the left (figs. 1, 2, 3).

There is a pair of well-developed median eyes in a single palpebral opening (figs. 1, 2, 10). A median conjoined auditory meatus is present (figs. 1, 2, 19). Eyes and ears on the outer sides are normal.

2. All of the tissues appear to have been in healthy condition when the embryo was killed.

3. Duplicity is more evident internally than externally, but bilaterality is strikingly apparent in all of the structures of the doubled region.

4. In the development of the teras the primitive morphological relationships and the normal embryonic flexures have remained undisturbed. The topographical changes in position of certain structures in the conjoined (median) region are apparently merely secondary, regulatory adjustments.

5. The morphological and teratological planes and axes are not necessarily identical.

6. The nervous system is well developed and proportionate to the size of the embryo.

7. The spinal cord is incompletely double and gives off laterally paired spinal nerves in normal manner (figs. 7, 20). Along the median ventral surface of the cervical cord a neural ridge gives off a short series of median (conjoined) spinal nerves, unganglionated and unbranched (figs. 5, 20).

8. The cervical sympathetic system is well developed on the normal sides. As in normal embryos, it consists of a stout truncus sympatheticus which parallels the trunk of the vagus nerve, curves dorsalward of the ganglion nodosum, and terminates in connective tissue medial to the petrosal ganglion of the glossopharyngeus (fig. 7). In addition, a shorter truncus between it and the normal spinal nerves connects it with them (fig. 7). In the median region the spinal sympathetic ganglia are poorly developed, being limited to a small patch of cells at the terminal end of the growing nerve trunks of the last two median spinal nerves (fig. 20, *s. 362*). The cranial sympathetic ganglia are present on the normal sides of the head members (figs. 15, 16, 17, 19). In the median region only the sphenopalatine ganglia were identified with certainty (figs. 13, 14). Ciliary and otic

ganglia are suggested, but with an uncertainty that warrants caution.

9. A pair of cerebral hemispheres, a diencephalon, and mesencephalon are normal for each head member. They diverge rostrally from the rhombencephalon (figs. 4, 6).

10. The rhombencephalon is conjoined, larger than in a normal embryo, but in proportion to the size of the teratological embryo (fig. 6).

11. The principal abnormalities of the head region are associated with the rhombencephalic region.

12. The conjoined metencephala form a 'mound' between the mesencephala (figs. 6, 8).

13. The central canal of the lower medulla, as seen in the sections, has the shape of an inverted Y (figs. 13, 14).

14. The fourth ventricles of the two head members are confluent (i.e., conjoined) and therefore larger than normal (figs. 9, 10). There is a lateral recess at each outer side, but none in the conjoined region (figs. 9, 10). An embryonic cerebellum bulges into the ventricle from the dorsal quadrants of the outer walls (figs. 5, 10), but no cerebellar swellings are apparent in the median region. The conjoined dorsal and ventral quadrants of the left and right halves of heads A and B, respectively, form a floor to the conjoined ventricles (figs. 9, 10). The quadrants lie side by side and are separated by a sulcus limitans, as are the dorsal and ventral quadrants of the normal (outer) sides (figs. 9, 10, 11). In the teras the ventral quadrants of the median region become increasingly larger toward the isthmi and bulge into the ventricle, and the dorsal quadrants correspondingly smaller and squeezed into the median line of the monster so that far rostrally the middorsal choroid plexuses of heads A and B lie dorsal and ventral to each other (fig. 8) and by their fusion form a narrow choroidal arch in the median sagittal plane of the metencephalic mound (fig. 5). A thin membrane forms the dorsal boundary of the broader portion of the ventricle, but on either side there is a well-developed choroid plexus extending into each lateral recess (figs. 9, 10).

15. The line of fusion of the two brains is thus determined to be along the external surface of the conjoined dorsal quadrants, which is also the median sagittal plane of the monster.

16. Twelve pairs of cranial nerves are present in normal linear arrangement on the outer sides of the teratological head (fig. 4). Only those branches which have relationship with the median region are considered in this paper.

17. Along the midline of the ventral surface of the conjoined rhombencephalon there are two cranial nerve-masses, spatially separated from each other and from the spinal neural ridge, and attached to the brain by bundles of nerve-root fibers (figs. 5, 6, 9 to 12). The more rostral one is concerned with median cranial nerves five, six, seven, and eight, and is designated the rostral cranial nerve-mass; the other is concerned with median cranial nerves nine, ten, eleven, and twelve, and is termed the caudal cranial nerve-mass.

18. The nerves of the median area are identified in part by their superficial origins and peripheral distributions, in part by their central connections. Nerves one, two, three, and four are not involved in the teratological considerations. The nerves identified by their central connections are given under paragraph 20. Those identified by their peripheral distributions are: a conjoined gasserian ganglion with attached ophthalmic nerve and its nasociliary infratrochlear branches to each head; conjoined abducens nerve to the external recti muscles of the median eyes; a conjoined geniculate ganglion (the median isolated ganglion) with a pair of great superficial petrosal and chorda tympani nerves, the infraorbital branches of the seventh nerve; median glossopharyngeus (?); median vagus, accessory, and hypoglossus (?).

19. The median isolated ganglion is identified with the seventh nerve, and not with the ninth or tenth as was suggested by Wilder ('08). The anatomical evidence establishes its identity as a conjoined geniculate ganglion (figs. 6, 14).

20. The central connections of the cranial nerves could not be determined in full. On the normal sides of the head there is no indication of abnormal behavior of the intracranial nerve

fibers, in so far as they could be followed. In the median region the course of the fibers is complicated by the altered form relations of the quadrants and the resulting topographical adjustments to size and shape. Nevertheless, *the normal pattern is clearly recognizable* and the following central connections are demonstrable: The motor roots of the two facial nerves from the genu internum to the rostral cranial nerve-mass (figs. 10, 11); with some uncertainty, the sensory roots and the motor nucleus of the conjoined trigeminus (fig. 9) and the acoustic fibers (fig. 9).

21. Heads A and B have each a median raphé with a clearly demonstrable sulcus limitans on either side of it as in a normal embryo (figs. 9, 10).

22. The fiber tracts of the outer sides are normal and readily identifiable, e.g., the tractus spinalis trigemini (figs. 11 to 15), tractus solitarius (figs. 11 to 13), and the fasciculus longitudinalis medialis (figs. 9 to 12). In the median region the fiber tracts are complicated by the altered form relations of the quadrants, as are the intracranial nerve fibers, but again, *the normal pattern is recognizable through the teratological alterations*. A greatly reduced spinal fifth tract is identifiable for the inner half of each head component for a considerable distance (fig. 9). A fasciculus longitudinalis medialis on each side of the median raphé of each head member is demonstrable for a long distance before fusion in the midline of the monster (figs. 9 to 15). This fusion adds another definite landmark of union of the two heads, for the two organisms are separate just as far as the fasciculi longitudinales mediales are separate. A conjoined tractus solitarius is demonstrable in the midline of the united dorsal quadrants in the conjoined medulla (figs. 13, 14, 15). The cerebral peduncles and posterior commissures are normal.

23. Summary of the conjoined structures: Rhombencephalon (figs. 5, 6, 8), fourth ventricle (figs. 9, 10), rostral and caudal cranial nerve-masses (figs. 5, 6, 9 to 14), median gasserian ganglion (fig. 10), median abducens nerve (not figured), median ninth, tenth, eleventh, and twelfth nerves (fig. 5), median spinal nerves (figs. 5, 18, 19, 20), median isolated geniculate ganglion (figs. 5, 6, 14), median tractus solitarius (figs. 13, 14), median

fasciculus longitudinalis medialis (fusion farther caudad than any of the figures). Of the non-nervous structures may be mentioned the terminal ends of the median submaxillary and sublingual glands (figs. 18, 19), cartilages of the external, middle, and internal ears of the median region (figs. 15 to 19), basis cranii (figs. 14, 15), and some of the cheek muscles. All of the conjoined structures receive contributions from the left half of head A and the right half of head B.

24. The dorsal quadrants of the juxtaposed halves of the two heads have been the most involved in the duplicity of the teras, and all the structures immediately associated with these quadrants have shared in the altered form relations; nevertheless the normal morphological and neurological pattern is clearly recognizable, and all of the anatomical evidence points toward a merely regulatory adjustment in a healthy, orderly developed, though teratological embryo, for wherever normality, or near-normality, can assert itself it is anatomically realized or approximated.

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Resumen por el autor, C. Judson Herrick.

El origen de los hemisferios cerebrales.

Admitiendo que el telencéfalo de los antepasados de los vertebrados es la porción más rostral del tubo neural, cuyas paredes no estaban complicadas por la presencia de espesamientos locales o evaginaciones, es evidente que en diferentes grupos de peces la diferenciación cerebral ha seguido varias líneas divergentes. En algunos Ganoideos (*Acipenser*, *Amia*) y en todos los teleósteos se ha evaginado una porción de la pared lateral del telencéfalo, adyacente a la lámina terminal, para formar el bulbo olfatorio, y el resto del telencéfalo se ha engrosado en diverso grado sin formar evaginaciones. Las porciones evaginadas son solamente los verdaderos hemisferios cerebrales, y el resto puede denominarse el telencéfalo medio o cerebro terminal primitivo.

En todos los vertebrados se pueden reconocer estas dos subdivisiones del telencéfalo, y desde las formas más inferiores a las más elevadas se une a los bulbos olfatorios una porción progresivamente mayor del cerebro terminal primitivo, el la porción evaginada de los hemisferios cerebrales. Algunas formas muy generalizadas de peces poseen, sin embargo, hemisferios cerebrales de paredes delgadas y extensamente evaginados, en vez de engrosamientos macizos locales en el cerebro terminal primitivo, y esta forma con cerebro de paredes delgadas puede haber estado mejor adaptada para oxigenar el cerebro en los peces primitivos que vivían en el fango de los lagos y corrientes en vías de desecación del periodo de aridez progresiva de la última era geológica de Siberia, de los cuales proceden los anfibios. Después de la adquisición de una respiración pulmonar en estos últimos, los hemisferios cerebrales evaginados, bien irrigados con sangre arterial, se diferenciaron progresivamente siguiendo direcciones imposibles en animales cuyo patrón del cerebro anterior se había estabilizado sobre el plan estructural de los Teleósteos.

A SKETCH OF THE ORIGIN OF THE CEREBRAL HEMISPHERES

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SEVENTEEN FIGURES

THE PRIMITIVE FOREBRAIN

From embryological and other evidence it may be assumed that the type ancestral to vertebrates possessed a central nervous system in the form of a neural tube with but little complication at the rostral end, comparable with that of larval *Amphioxus*. In response to the peripheral differentiation of eye and nose, two pairs of lateral evaginations of the walls of the neural tube probably took place early in vertebrate evolution, namely, the optic vesicles and the olfactory bulbs, the first from the betweenbrain (diencephalon), the second from the endbrain (telencephalon). The embryological evidence suggests that the optic evagination occurred earlier in phylogeny than the olfactory; at any rate, it always precedes in ontogeny.

In all adult vertebrates the cavities of the original evaginations of the optic vesicles have been nearly or quite obliterated, and the retinas and so-called optic nerves very early in vertebrate evolution attained stable and definite form. The cerebral correlation center for visual reflexes is primarily in the midbrain, with very small collateral connections (in cyclostomes and Ichthyopsida) in the thalamus. The progressive enlargement of the thalamic optic centers in Sauropsida and Mammalia is correlated with the elaboration of the cerebral cortex.

The internal structure of the olfactory bulbs is also in principle similar throughout the vertebrate series; but the differentiation of the secondary olfactory correlation centers at the bases of the olfactory bulbs, which in the lower forms compose prac-

tically all of the endbrain, has been effected in so diverse ways as to present one of the most remarkable series of evolutionary changes known in biology. It is to this series of events that I wish to direct attention.

In embryos of fishes and amphibians shortly after the closure of the neural tube we find a stage of great interest in the analysis of the probable functional factors operating in early stages of the evolution of the cerebral hemispheres. In teleosts at the stage shown in figure 1 the optic vesicles have evaginated from

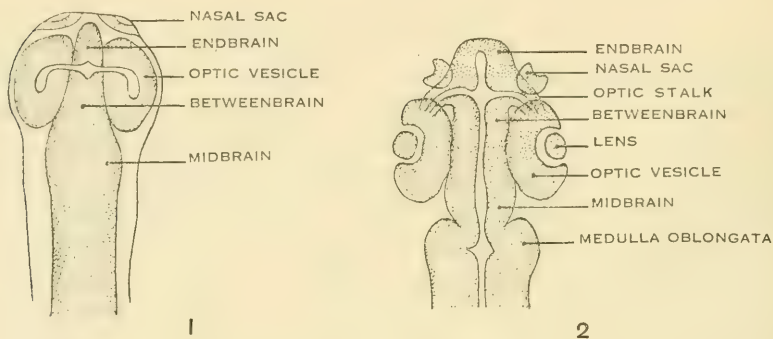


Fig. 1 Surface view of the head end of a 33-hour embryo of the sea-bass (*Serranus atrarius*) from the dorsal side, illustrating the evaginated optic vesicles and the small (and still solid) endbrain. Modified from H. V. Wilson ('91, fig. 146).

Fig. 2 Surface view of a 62-hour embryo of the sea-bass illustrating the primitive endbrain with thickened lateral walls in close contact with the nasal sacs. Modified from H. V. Wilson ('91, fig. 149).

the neural tube and their cavities communicate with the third ventricle through the hollow optic stalks (precursors of the optic nerves). The endbrain is a very small rudiment. In a later stage, as illustrated in figure 2, the eyes have differentiated further and the endbrain has enlarged somewhat. In each lateral wall of the latter region there is a thickening which represents an accumulation of embryonic nervous tissue from which will develop the adult olfactory bulb and the olfactory correlation centers lying behind it. There is as yet no evagination of any part of the walls of the endbrain. In later stages the anterior

part of this thickened region will evaginate to form hollow olfactory bulbs (as in figs. 3 and 4).¹

Figure 3 illustrates in a schematic way a condition of the fore-brain which may be taken as a point of departure for a consideration of the diverse directions taken in the further evolution of this region in different vertebrates.

Here the endbrain has departed but little from the primitive relations of a simple neural tube save for the evagination of an

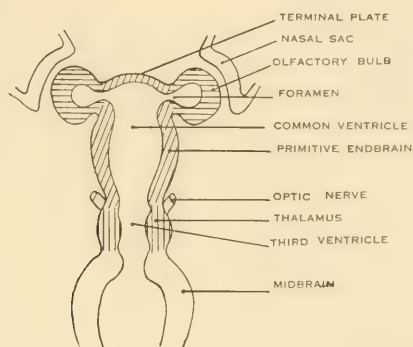


Fig. 3 Diagram illustrating the probable primitive vertebrate type of fore-brain as seen in longitudinal section. A portion of the endbrain behind the terminal plate has evaginated in correlation with the differentiation of the adjacent nasal organ and olfactory nerve. This forms the olfactory bulb which comprises the entire cerebral hemisphere. The cavity of the olfactory bulb is the lateral ventricle. The remainder of the endbrain is unevaginated (primitive endbrain).

In this and the following diagrams the cut surfaces of the walls of the neural tube are conventionally marked, as follows: primitive endbrain, diagonal lines; evaginated endbrain (cerebral hemispheres), horizontal lines; betweenbrain, vertical lines; midbrain, unshaded.

olfactory bulb on each side close behind the terminal plate. This evaginated portion of the neural tube lies closely apposed to the nasal sac. In this diagram we can recognize two subdivisions of the endbrain: 1) an unevaginated portion which may be called the telencephalon medium or primitive endbrain, and

¹ In this connection I am not unmindful of the very atypical development of the central nervous system of teleosts in early stages; but the originally solid nervous cord is early transformed into a neural tube whose subsequent development is comparable with that of other vertebrates.

2) an evaginated portion, the cerebral hemispheres, which in this case are composed of the olfactory bulbs only. The primitive endbrain contains an unpaired ventricle, the common endbrain ventricle, which is always bounded in front by the terminal plate and in forms above the fishes is the terminal part of the third ventricle as the latter cavity is usually defined. Each cerebral hemisphere contains one of the lateral ventricles which communicates with the common ventricle by an interventricular foramen (of Monro).

The endbrain of every vertebrate is organized on this plan, with, however, the greatest diversity of detail. As we pass from lower to higher forms, there is in the broad view a progressive incorporation of more and more of the tissue of the original unevaginated primitive endbrain into the evaginated cerebral hemispheres, though always, even in the adult human brain, there is a small residue of unevaginated endbrain tissue between the optic chiasma and the terminal plate (the preoptic nucleus) and a residual portion of the common ventricle in the preoptic recess (Johnston, '11, p. 50; '11 a, p. 496; '12, p. 367).

The different vertebrate phyla present a varied assortment of deviations from the paradigm or schematic pattern just described, but in no case is the pattern fundamentally changed. Some illustrations of these lines of divergent specialization will be cited.

TYPES OF FOREBRAIN IN FISHES AND AMPHIBIA

In the adult sturgeon, *Acipenser*, the departure from the schematic type is very slight, consisting mainly in the thickening of the side walls of the primitive endbrain, thus providing space for the neurons of the correlation centers which receive the great descending olfactory tracts from the olfactory bulbs. These relations are illustrated in figure 4, which presents a diagrammatic longitudinal section of the forebrain of the sturgeon so taken as to reveal the relations of the brain walls to the contained ventricles (Johnston, '01). Figure 5 shows a transverse section through the primitive endbrain.

The bony ganoids, as illustrated by *Amia*, and their allies, the teleosts, have gone to the limits of extreme specialization in this direction. In late embryonic stages the condition is substantially as figured for the sturgeon, but in the adults of some

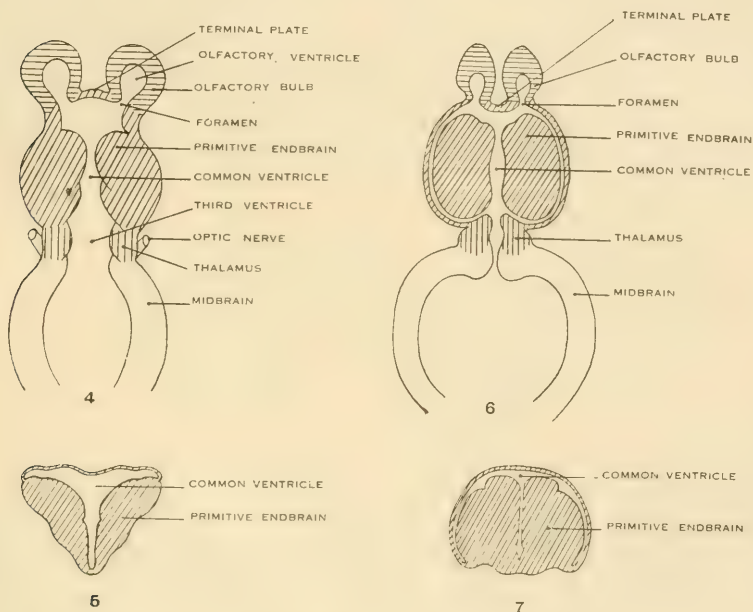


Fig. 4 Diagrammatic longitudinal section of the forebrain of the sturgeon, *Acipenser*. The cerebral hemispheres comprise only the olfactory bulbs, the remainder of the endbrain being unevaginated, but thickened laterally.

Fig. 5 Cross-section through the middle of the thickened primitive endbrain of the sturgeon. Figures 4 and 5 are based on the figures of Johnston ('01).

Fig. 6 Diagrammatic longitudinal section through the forebrain of a teleost. As in the sturgeon, the true, evaginated cerebral hemispheres contain only the olfactory bulbs, below which there are great thickenings of the unevaginated primitive endbrain, which arise first embryologically in the side walls, as in the sturgeon, but in the adult are attached only to the floor.

Fig. 7 Cross-section through the thickened primitive endbrain of a teleost.

of the species the lateral thickenings have enormously increased so that they bulge upward into the common ventricle and are attached only on the ventral side, as illustrated in figures 6 and 7. These thickenings are sometimes infelicitously called cerebral

hemispheres. The true hemispheres, as the diagram (fig. 6) shows, are represented only by the evaginated olfactory bulbs.

The thickenings of the primitive endbrain of teleosts have been described as everted in contrast with the extensively evaginated hemispheres of Amphibia, but this is hardly an adequate statement of the case. It is no doubt true that there has been some lateral eversion of the wall analogous with that so strikingly shown by *Polypterus* (fig. 11). But Sheldon ('12) has shown that the teleostean form has not been reached by a simple bending of the massive lateral wall outward, as is clearly the case in

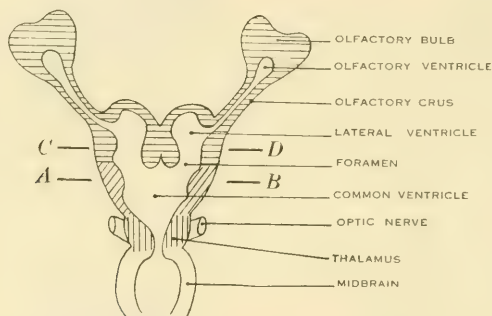


Fig. 8 Diagram of the relations of the walls of the forebrain and its ventricles in the dogfish, *Squalus acanthias*. The line A-B indicates the plane of section of figure 9; C-D that of figure 10.

The relations of these ventricles are quite different from those of *Mustelus canis*, as figured by Johnston ('06, fig. 8), but they conform closely to his diagram ('06, fig. 9) "to show what is believed to be the primitive relations of the wall of the ventricle."

Polypterus, but chiefly by the accumulation of additional nervous tissue in the middle of the wall with more or less plastic rearrangement of the component nerve centers.

The elasmobranchs, as illustrated by the dogfish, *Squalus acanthias* (figs. 8, 9, and 10), show a different arrangement of the correlation centers at the bases of the widely evaginated olfactory bulbs. The thickening here takes place chiefly in and adjacent to the terminal plate, a considerable part of the thickened tissues lying above the ventricle and hence not shown in figure 8 (cf. figs. 9 and 10). At the base of the olfactory bulb

there is a considerable amount of evaginated tissue which is continuous with the unevaginated primitive endbrain behind the wide interventricular foramen. The hemisphere, therefore, contains the fully evaginated olfactory bulb and some adjacent tissue which is not sharply marked off from that of the unevaginated primitive endbrain.

Both elasmobranchs and teleosts are very efficient types of fishes. Biologically they dominate their respective environments. This dominant position, however, has been brought about by very precise adaptation of each individual species to a particular habitat and mode of life on the reflex plane, rather

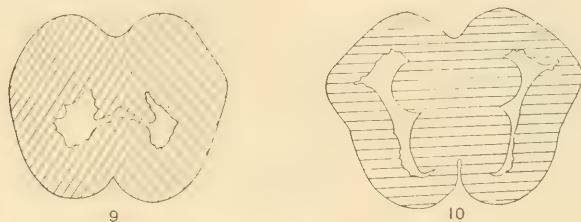


Fig. 9 Cross-section through the primitive endbrain and common ventricle of *Squalus acanthias* in the plane A-B of figure 8. The lateral dilations of the common ventricle are continued forward into the lateral ventricles; the large masses above the ventricle are continued forward into the cerebral hemispheres (cf. fig. 10). Modified from Johnston ('11, fig. 54).

Fig. 10 Cross-section through the cerebral hemispheres of *Squalus acanthias* in the plane C-D of figure 8. Modified from Johnston ('11, fig. 57).

than by an increase in capacity for individual adjustment to diverse and variable conditions. And neither group has given rise to anything higher. They form terminal branches of the phylogenetic tree. These types of forebrain appear to be incapable of expansion in directions affording greater flexibility and modifiability of behavior of the individual.

The forebrain of *Polypterus*, the most primitive of existing ganoids, is in some respects very close to the architypical form illustrated in figure 3, but in other respects it is aberrant. *Polypterus* is unique among living fishes, not only in forebrain structure, but in other respects also. By the systematists it is widely separated from the other members of the old group of so-called

ganoid fishes, a group which, though retained in popular usage, is now without scientific status. Paleontologists follow the branch of 'lobe-finned ganoids' containing *Polypterus* back to a common origin with the lungfishes and far removed from the forms ancestral to the other groups of recent fishes (Osborn, '17, fig. 50, p. 168).

In *Polypterus* the olfactory bulbs are fully evaginated and the primitive endbrain is greatly elongated. The side walls are

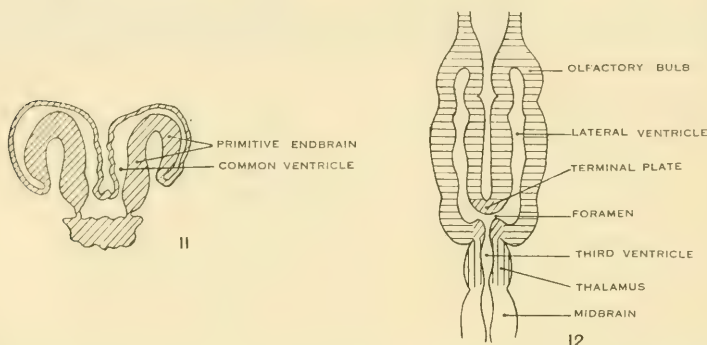


Fig. 11 A transverse section through the primitive endbrain of *Polypterus* bichir between the terminal plate and the betweenbrain. The thin but massive side walls are everted and the wide common ventricle is roofed by membrane only. The median longitudinal fold of the roof accentuates the illusory appearance of distinct cerebral hemispheres similar to those of *Protopterus* (fig. 13), but there is no real resemblance. Redrawn after Waldschmidt ('87, fig. 4).

Fig. 12 Diagrammatic longitudinal section of the forebrain of *Protopterus*, illustrating the fully evaginated cerebral hemispheres. The figure is based on the drawings of Burekhardt ('92) and is purely schematic.

massive and the roof membranous, as in the sturgeon (figs. 4, 5), but the massive walls are thin and strongly everted, as shown in figure 11. When the membranous roof is stripped off, the appearance of this brain seen from the dorsal side presents a superficial resemblance to that of *Protopterus* (figs. 12, 13), but the resemblance is wholly illusory, for no part of the endbrain of *Polypterus* behind the olfactory bulbs is evaginated and the elongation of the so-called hemispheres is altogether behind the terminal plate.

In the lungfishes, on the other hand, there is a tendency for the entire endbrain behind the olfactory bulbs to evaginate laterally. In *Ceratodus* (Bing and Burekhardt, '05) the form suggests that of the selachian forebrain, though with more extensive lateral outpouching, with less thickening of the walls in the vicinity of the terminal plate, and with many other differences. The thin lateral walls of the primitive endbrain are bowed outward (not everted) and, as in *Polypterus*, they are connected with each other dorsally for their entire length by a plexiform membrane, thus enclosing a wide common ventricle. The lateral outpouching (exclusive of the olfactory bulb) extends but little, if at all, rostrally of the terminal plate and there is



Fig. 13 Cross-section through the cerebral hemispheres of *Protopterus* between the olfactory bulbs and the terminal plate. Redrawn from Burekhardt ('92, fig. 23).

no sagittal fissure separating two cerebral hemispheres behind the olfactory bulbs. The true (fully evaginated) cerebral hemisphere, accordingly, contains only the olfactory bulb.

The brains of *Lepidosiren* and *Protopterus* (figs. 12, 13) resemble each other closely, and in these cases the larger part of the side wall of the primitive endbrain has joined the olfactory bulb to form a fully evaginated cerebral hemisphere. This results in the formation of extensive, hollow, thin-walled hemispheres separated by a deep sagittal fissure, whose rostral ends are formed by the olfactory bulbs and whose remaining parts include tissues which in most other fishes are represented in the unevaginated primitive endbrain. These evaginations are protruded forward far beyond the terminal plate.

This type of brain with extensive hollow cerebral hemispheres, though perhaps no more efficient as a neuromotor apparatus.

than those of other fishes (in fact, probably from some points of view less so in these species), nevertheless has potentialities of further differentiation from which the other types are apparently forever excluded.

The paleontological evidence seems to be clear that the ancestors of the Amphibia were primitive ganoids of the general type illustrated by *Polypterus* and that the Dipnoi arose from a closely related stock. The forebrains of the existing members of these groups are all characterized by thin nervous walls and elaborately developed membranous parts. But little is known of their histological structure, but evidently this is very simple and primitive. The forebrains of *Polypterus* and *Ceratodus* have deviated in form from the primitive pattern in directions very divergent from that shown by the Amphibia. On the other hand, the resemblance of *Protopterus* and *Lepidosiren* in this respect to the generalized Amphibia is very close. It is, therefore, very probable that the primitive ganoidean ancestor of amphibians had a forebrain closer to that of *Protopterus* than of any other surviving type.

Turning now to the brains of the Amphibia (figs. 14, 15), the resemblance between their forebrains and those of *Protopterus* and *Lepidosiren* is very close indeed. In the relatively thin-walled cerebral hemisphere the various correlation centers of the endbrain, which serve primarily as apparatus of the different forms of response to olfactory stimuli and for compounding these with other forms of sensory excitation, may enlarge without crowding by simply expanding the size of the hemispheric vesicle. And this they have done, to a notable degree in the Amphibia and in still larger measure in the classes which have been derived from them.

THE CYCLOSTOME FOREBRAIN AND ITS HISTOLOGICAL STRUCTURE

The cyclostomes occupy a peculiar position in the vertebrate series. Though undoubtedly aberrant, they probably arose from extinct types which were close to the roots of the vertebrate genealogical tree. Their brains will next be considered.

The forebrain of the lamprey (fig. 16) suggests in its form an approach to the selachian condition, though the resemblance is not close. The olfactory organ is large and the olfactory bulb is fully evaginated. The cerebral hemisphere contains behind the bulb a smaller olfactory lobe whose homologies in other vertebrates are by no means clear; resemblance to the lateral olfactory nucleus complex of higher forms is suggested, though this homology is not certain. The primitive endbrain and betweenbrain are in very generalized condition, though the more

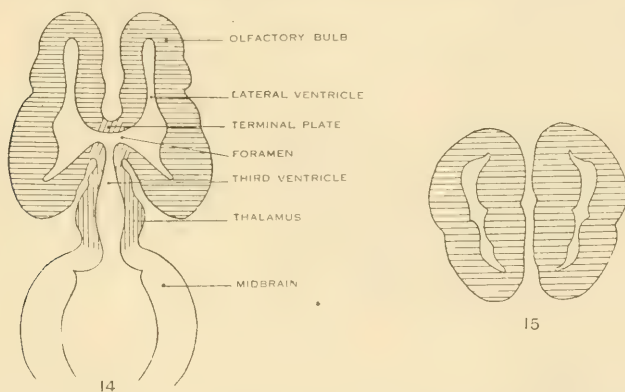


Fig. 14 Diagrammatic longitudinal section of the forebrain of an amphibian. The larger part of the endbrain has been evaginated to join the olfactory bulbs in the formation of the hollow cerebral hemispheres, whose walls are nowhere greatly thickened.

Fig. 15 Cross-section through the amphibian cerebral hemispheres in front of the terminal plate.

important regions of higher forms can be identified (Johnston, '02, '12; Herrick and Obenchain, '13).

The feature of the cyclostome brain of greatest interest from the standpoint of this sketch is the histological structure. This is exceedingly primitive and generalized. Throughout the brain the cell bodies of the neurons are in the original embryonic position as a layer of central gray matter bordering the ventricular cavities. Their dendrites and axons are directed outward, where they form a superficial layer of white matter within which all

fiber tracts and synaptic connections are found. Most of these neurons are of undifferentiated form, and the various groups of neurons performing similar functions (the so-called cerebral nuclei) are very incompletely separated from each other. The nerve fibers are for the most part diffusely scattered in the white layer with few clearly defined tracts.

The sense organs and peripheral nerves of cyclostomes are simply organized, but the pattern is in its broad outlines similar to that of the true fishes (Johnston, '05). Within the brain, however, the primary sensory nuclei into which the various sensory components of the cranial nerves (from skin, internal

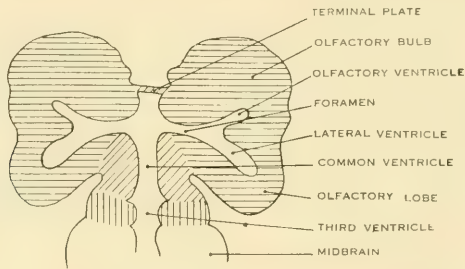


Fig. 16 Diagrammatic longitudinal section through the forebrain of the lamprey, *Petromyzon*, illustrating the form of the cerebral hemispheres. The hemispheric evagination includes a large olfactory bulb and a smaller olfactory lobe, leaving a considerable residue of tissue in the unevaginated primitive endbrain.

ear and lateral-line organs, taste buds, etc.) discharge their nervous impulses are far less sharply separated than in the true fishes. And in the higher correlation centers there is little precise localization of the functional areas. All forms of peripheral sensory excitation tend to converge into relatively few final common motor paths which are very simply arranged.

From this arrangement of the conduction paths and nerve centers it follows that the nervous organization is such as to make possible a relatively small number of reactions to all sorts of sensory stimulation and that these reactions are for the most part simple total movements of the whole body rather than complex adjustments involving precise coördination of many

separate organs. Observation of the behavior of cyclostomes shows that this is, in fact, their type of action system.

This histological pattern of the cyclostome brain is in sharp contrast with that of most of the true fishes and especially of the teleosts, where the various functional systems of neurons are segregated into as well-defined nuclei and fiber tracts as are those of the brain stem of mammals. The histological pattern of the cyclostome brain may without question be regarded as typical of the primordial vertebrate ancestor. It is unspecialized, plastic, and capable of differentiation in any direction.

It may be assumed that, if the gnathostome vertebrates arose from some primitive extinct type of cyclostome (as is the current belief), the cerebral histological pattern of this ancestral form was not more highly differentiated than is that of modern cyclostomes. The history of the evolution of the brain from such an ancestral form, through the primitive ganoids to the Amphibia, cannot at present be written with satisfactory assurance. More detailed knowledge of the internal structure of the brains of the most generalized existing ganoids (*Polypterus* and its allies) would probably contribute important evidence, and this is a most inviting field for future research. Johnston's detailed study of the internal structure of the brain of *Acipenser* ('01) gives helpful insight into a nervous system but little more highly organized.

STRUCTURE AND DEVELOPMENT OF THE AMPHIBIAN HEMISPHERE

Fortunately, the Amphibia themselves can supply the missing links in their own phylogensis with a high degree of probability. Modern Amphibia, it is true, are aberrant forms and some are probably retrograde. But the larvae of all species are very similar and they come to functional development earlier in the ontogeny than do most other vertebrates, thus permitting direct observation of the changes in histological pattern of actively functioning reflex systems from the simplest possible form to the considerable complexity of the adult anuran brain (Herriek and Coghill, '15). Moreover, the adults of the various urodele

species illustrate arrests at different stages in this developmental process. Even though the very generalized forms like *Necturus* give evidence of retrogression, yet the definitive histological pattern of the adult brain is strikingly similar to that of larvae of other forms and of adult cyclostomes. The histological structure of larval urodeles and of adult *Necturus* has been described in considerable detail (Herrick, '14, '14 a, '17) and that of the tadpoles of the frog is probably essentially similar.

From these considerations it is probable that the line of descent through extinct ganoidean types to the earliest Amphibia of the Devonian was generalized not only as regards the external form of the brain, but also in its histological structure. The preservation of this plastic, undifferentiated, or 'young' type of tissue was doubtless an essential factor in making possible progressive evolution in the new amphibian direction when the time was ripe for this evolutionary movement.

In the meantime most of the other groups of fishes referred to in this sketch had diverged from the generalized ancestral form of vertebrate brain, not only in the form relation of the forebrain already described, but also in the direction of much more highly specialized histological structure. Their tissues were matured or 'senile' in the sense defined by Child ('15). The establishment of the sharply circumscribed and rigid reflex patterns characteristic of the various species of higher fishes stabilized their organization at the expense of plasticity and thus determined the direction of future evolution of each phylum within certain wide limits. Dedifferentiation permitting a new start in a different direction was a biological impossibility. The probable mechanism of this orthogenetic trend I have elsewhere discussed ('20).

The amphibian hemisphere is evaginated on a quite different plan from that of the selachians already described. In the sharks (and more conspicuously still in *Chimaera*) the most highly developed secondary olfactory centers are found as close as possible to the bases of the fully evaginated olfactory bulbs. The terminal plate and adjacent regions are greatly thickened (figs. 8, 9, 10), and the hollow cerebral hemispheres described in this

region are formed not merely by evagination of the lateral wall of the neural tube, but also by thickening of the walls in situ, and especially of the terminal plate, thus separating the terminal part of the common ventricle into two lateral ventricles with a minimal amount of true evagination. The caudal part of the endbrain is much less highly differentiated, especially in the lower types of elasmobranchs.

Examination of the development of the cerebral hemispheres of the Amphibia, taking *Amblystoma* as a type, shows a very different history. Early larvae in Coghill's non-motile stage show no evagination of the walls of the endbrain, but instead the lateral walls are thickened. Immediately external to these thickenings are the developing nasal sacs, the arrangement being similar in principle to that described above for teleosts (fig. 2). In immediately following stages evagination of the hemispheres begins and in the 10-mm. larva, which is an active swimmer, this evagination is well advanced.

The evagination of the amphibian hemisphere, however, does not begin at the site of the future olfactory bulb, but at the extreme caudal end of the endbrain just in front of the velum transversum. This region, which forms the posterior pole of the hemisphere, is well evaginated before there is any notable outpouching in the more rostral part of the endbrain close to the lamina terminalis which lies adjacent to the nasal sac and which will later form the olfactory bulb.

A somewhat similar condition prevails in *Lepidosiren*, as shown by Graham Kerr's illustrations ('02, fig. 10); but in this case the peculiarity in question is correlated with the fact that the olfactory bulb develops not at the rostral end of the primitive endbrain, but on the dorsal border near its caudal end in immediate contact with the nasal sac. These relations are shown in figure 17. In relatively late stages the olfactory bulb shifts its position to become terminal in the hemisphere. Whether this peculiar condition in *Lepidosiren* is indicative of a similar feature in the ancestors of the Amphibia it would be rash to say; certainly it is possible that the primitive position of the olfactory evagination

in this phylum was at the caudal end of the endbrain rather than adjacent to the terminal plate, as in most other fishes.

The initial functional impulse for the differentiation of the endbrain was undoubtedly the excitations arising in the nasal epithelium, and the precocious evagination of the region of the posterior pole in the Amphibia may be explained, as just suggested, by a more caudal position of the nasal sac in the precursors of this phylum than in most types of fishes, or there may be some other factor not yet recognized.

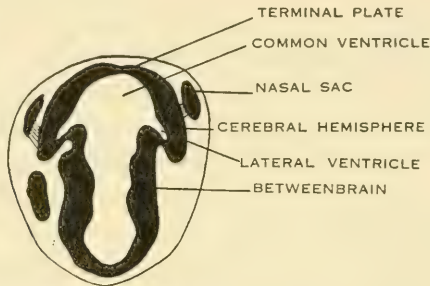


Fig. 17 Diagram of a horizontal section through the forebrain of fetal *Lepidosiren* (Graham Kerr's stage 30), illustrating the relations of the nasal sacs to the hemispheric evaginations. Olfactory nerve fibers are seen connecting the nasal sacs with the posterior parts of the evaginations of the lateral walls of the endbrain. Redrawn from Elliot Smith ('08, fig. 4).

FOREBRAINS OF MUDFISHES

As we have seen, the most characteristic difference between the forebrains of the Amphibia and those of the various groups of highly specialized fishes lies in the more complete evagination of the primitive endbrain into the cerebral hemispheres in the Amphibia. And we next inquire what were the reasons—adaptive, physiological, mechanical, or other—leading up to this departure from the directions taken by the higher fishes.

First of all it should be borne in mind that the movement in this direction was not confined to the Amphibia. We find to-day fully evaginated hemispheres in two species of lungfishes. Probably the trend in this direction began in the ganoidean stem ancestral to both Dipnoi and Amphibia.

Now these forms are not the most successful types of fishes. From the standpoint of biological efficiency they are surpassed by the elasmobranchs which from early Silurian times have dominated the salt waters and by the teleosts which dominate the fresh waters and now compete with the sharks for the mastery of the oceans. The surviving members of these archaic types exist to-day not by reason of the functional superiority of their hollow cerebral hemispheres over the massive solid thickenings of the primitive endbrain seen in teleosts, but rather because they have, as it were, hidden themselves away in crannies of the environment not sought after by the more enterprising groups of fishes. And here perhaps is the solution of our problem.

Fishes with evaginated cerebral hemispheres are inhabitants of sluggish waters; they and their allies, the primitive ganoids, are mudfishes. Lull ('18) has called attention to the fact that this type of fishes came into prominence at a geological period (the late Silurian and early Devonian) when extensive continental fresh-water lakes and streams were drying up. The fish fauna of these waters was faced with the alternative of gradual modification in adaptation to seasonal drought or extinction. The more highly specialized species inhabiting these stagnant waters undoubtedly perished, as their 'senile' type of organization was unable to make the necessary readjustment; but the more generalized forms, whose undifferentiated tissues retained the plasticity and adaptability of the 'young' type, met the emergency by supplementing their water-breathing apparatus by air-breathing organs of various sorts. Thus arose the lungfishes and the Amphibia.

Most of the profound modifications of the vertebrate body necessitated by the transfer from the aquatic habitat to land can readily be understood. The adaptive value of lungs, limbs, etc., is obvious; and, given variations of appropriate range in a plastic type, the metamorphosis may be conceived as carried through in accordance with the principle of survival of those variations most fit to meet the changed conditions. But the reason for the association of evaginated cerebral hemispheres with the other and obviously adaptive characters related with

air breathing is not so evident. Nevertheless, this collocation seems to have been actually realized. I am not prepared to offer a satisfactory solution of this problem, though the following suggestions may be presented for further consideration and criticism.

For fishes living in imperfectly aerated water the oxygen supply of the brain is a vital matter. The arteries of the brains of fishes are derived from the internal carotid, which brings freshly aerated blood directly from the gills (see the description of the cerebral arteries of *Ceratodus* by Bing and Burekhardt, '05). This vascular supply to the brains of lungfishes is very rich, as indicated by the following comment by Graham Kerr ('02, p. 428):

In dissecting the brain of *Lepidosiren* one is struck by the extraordinary development of richly ramifying blood-vessels within the cranial cavity, forming a packing all round the brain. This may possibly be an adaptation to the times at which it is impossible to make the blood rich in oxygen, during the final stages in drying up of the swamps, or during casual rainfalls in the dry season.

The brains of lungfishes and all of the more generalized ganoids are, moreover, provided with extraordinarily enlarged choroid plexuses which probably ensure the highest possible oxygen supply to the cerebrospinal fluid within the brain ventricles and in the surrounding endocranial spaces. Obviously, this arrangement is well adapted to make the largest possible use of a deficient supply of oxygen, for the nervous tissues can take up oxygen directly from the blood-vessels which envelop and penetrate their mass and also from the cerebrospinal fluid by which they are bathed. But the latter source of oxygen is available only on the ventricular and external surfaces, and the interior of any considerable thickenings such as characterize the fore-brains of teleosts would be dependent upon a single source of oxygen only, viz., the penetrating blood-vessels. This latter source is obviously adequate for species living in well aerated water, but for mudfishes, and especially those subjected to periods of drought, the interior of such thick masses might suffer asphyxi-

ation without the collateral source of oxygen furnished by the cerebrospinal fluid.

The thin walls of the forebrains of *Polypterus* and the lungfishes, accordingly, have two possible sources of oxygen supply, in contrast with the thickened masses of the brain of teleosts which have but one, and if the supply is deficient this may be sufficient to maintain the life of the tissue during critical periods of drought. Indeed, in the total suppression of gill breathing skin respiration may be adequate to supply the minimal amount of oxygen necessary to keep such a brain alive while the animal remains inactive. This minimum of oxygen might well be quite inadequate to prevent asphyxiation of a brain of teleostean type.

Now the form of the forebrain is not an essential factor in this situation in the case of lowly organized fishes of sluggish habit, provided only that the walls are thin and highly vascular and there are extensive choroid plexuses. The everted primitive endbrain of *Polypterus*, the dilated form of *Ceratodus*, and the evaginated cerebral hemispheres of *Protopterus* and *Lepidosiren* appear to be equally competent to meet the harsh conditions imposed. But only in the evaginated forms does there reside the potentiality of indefinite further differentiation under more fortunate conditions of life.

On the basis of these considerations it may be assumed that a primitive ganoid type in late Silurian or early Devonian times, whose brain form was not far from that indicated in figure 3 or that of the modern petromyzonts and whose histological structure was primitive and generalized, was subjected to periodic drouth. This climatic change is believed to have been very pronounced and widespread at this time (Lull, '18, p. 121). In adaptation to this environmental change the forebrain of the generalized type in question differentiated in one or several of the directions presented by modern ganoids and lungfishes. One such form, viz., the thin-walled evaginated hemisphere, proved capable of further progressive differentiation in air-breathing Amphibia and in their later descendants.

By reason of the limitations imposed by their modes of life these animals in the early stages of this differentiation undoubt-

edly remained on a low level of organization, as do the modern mudfishes, passing a sluggish and uneventful existence. But with the elaboration of an efficient pulmonary respiratory mechanism (which indeed is only imperfectly realized in many living urodele Amphibia), these limitations were removed; the oxygen supply of the brain was adequate, and the evaginated type of cerebral hemisphere, acquired during a period when the vital currents were at lowest ebb, develops possibilities of further evolutionary advance forever denied to those types of fishes which diverged in other and (for fishes) more favorable lines of specialization.

THE CORRELATION CENTERS OF THE FOREBRAIN

Having now reviewed some of the various forms exhibited by the forebrains of different groups of Ichthyopsida and suggested some of the physiological factors which may have been operative in the establishment of the fully evaginated type of cerebral hemispheres found throughout the Amphibia and all higher forms, it remains to consider briefly some other functional influences which have played a very different rôle in shaping the anatomical configuration of this region. I refer to the directions taken by the internal conduction pathways and the connections which these make among themselves in the various correlation centers. Here we can base our conclusions on the firm ground of comparative anatomical facts, with satisfying confidence in their validity.

Without here going into the details of these connections, they obviously comprise two great systems of tracts, first, the descending olfactory system, and, second, the non-olfactory ascending systems.

The olfactory system comprises: 1) peripheral neurons of the first order arising in the nasal epithelium and ending in the glomeruli of the olfactory bulb; 2) neurons of the second order, the mitral cells of the bulb, whose axons form the olfactory tracts ending in the nuclei of the secondary olfactory area (often called the olfactory lobe); 3) neurons of the third order arising

in the olfactory area and terminating either in various higher correlation centers or in reflex centers of the betweenbrain and midbrain. The tracts of the third order are usually named by hyphenated compound words, of which the second member designates the place of termination, such as tractus olfacto-habenularis, tractus olfacto-corticalis, etc.

It is probable that primitively the olfactory area was an undifferentiated secondary olfactory nucleus extending backward from the base of the olfactory bulb and receiving various ascending non-olfactory systems from the betweenbrain. A remnant of this primitive undifferentiated nucleus persists in all vertebrates at the base of the olfactory bulb, in most cases extending outward more or less into the bulb, and is called the anterior olfactory nucleus. The remainder of the olfactory area has been differentiated in conformity with the specificity of the various ascending systems of fibers into the several olfactory nuclei, each of which is concerned with a particular complex of correlations between olfactory nervous impulses, on one hand, and certain non-olfactory systems, on the other hand, thus giving rise to the lateral, medial, and intermediate olfactory nuclei and their subdivisions.

The regional differentiation of the anatomically distinct centers of the entire endbrain behind the olfactory bulbs, therefore, primitively arose as a result of the invasion of the original secondary olfactory area by diverse non-olfactory systems, and the entire history of the subsequent evolutionary differentiation of this part of the brain can be written in terms of the interaction of these two systems of conduction fibers—those descending from the olfactory bulb and those ascending from the betweenbrain. Increasingly complex correlations between the olfactory centers in front and the non-olfactory centers of the midbrain led to the forward growth of tracts from the lower reflex centers of touch, taste, vision, hearing, etc., into the olfactory territory of the endbrain (and probably in still earlier stages the ascending tracts into the betweenbrain were led forward by the same motive).

The details of this dramatic history cannot be recounted here. In a general view of the process it may be said that in cyclostomes the entire endbrain and a large part of the betweenbrain are dominated by the olfactory system, the non-olfactory components entering this territory from the midbrain being relatively small and incompletely known. As we ascend the vertebrate scale the non-olfactory systems assume progressively greater importance. In urodeles a considerable part of the thalamus is devoted exclusively to non-olfactory correlations, but no part of the cerebral hemispheres is wholly free from olfactory connections. In reptiles the ascending systems are greatly enlarged and a portion of the corpus striatum complex appears to be devoted exclusively to them. Here there is well-defined cerebral cortex, most of which is clearly dominated by its olfactory connections (hippocampus and pyriform lobe), though in another part (the general cortex) somatic systems predominate (Elliot Smith, '10, '19). In mammals somatic systems with no admixture of olfactory elements come to dominate the architecture and functions of the cerebral hemispheres, until in man, whose olfactory organs are greatly reduced, the olfactory centers are crowded down into relatively obscure crannies of the hemisphere by the overgrown somatic systems.

CONCLUSION

In summary, it may be regarded as established that the terminal portion of the neural tube early in vertebrate evolution gave rise to two pairs of lateral evaginations in correlation with the differentiation of the two sense organs which serve as the most important distance receptors, namely, the optic vesicles and the olfactory bulbs. In the most primitive living vertebrates almost all of the brain in front of the midbrain is dominated by the olfactory system and the differentiation of this region in all higher forms appears to have taken place largely under the influence of various systems of non-olfactory fibers which have grown forward into this olfactory territory. Increasingly complex correlations of the various other senses with smell have

involved the elaboration of separate correlation centers in the forebrain for each of these reflex patterns, different in each species of animal according to its mode of life. The diverse patterns of cerebral architecture exhibited in the vertebrate series are, therefore, structural expressions of these functional relationships, namely, the various parts played by the olfactory and the different non-olfactory sensory systems.

The form relations of these correlation centers which have been assumed by the different groups of fishes are exceedingly diverse, each structural pattern probably reflecting some particular grouping of the sensorimotor elements of behavior characteristic of the species. It would almost seem as if nature had tried many experiments, each of which was successful within a certain environmental range. For life in an aquatic medium the most successful of these appears to have been the teleostean type; but this type, though capable of unlimited modification of detail on the plane of relatively simple forms of reflex behavior, has not proved adequate for differentiation in the direction leading up to the individually modifiable and intelligent forms of behavior.

Moreover, none of the more highly specialized kinds of fishes were able to make the structural readjustments required to maintain themselves in inland waters during the period of continental elevation and consequent drouth known to have occurred in late Silurian times. On the other hand, certain very generalized species of ganoids were able to survive these periods of desiccation by developing accessory respiratory organs and so modifying the brain and its membranes as to facilitate its aeration in a reduced supply of oxygen. Of the several modifications of brain form which met the requirements of these adverse conditions, one in particular has proved susceptible of unlimited further differentiation.

Those primitive ganoids of Silurian or early Devonian times which were able to perfect the air-breathing apparatus and so to leave the water as amphibians probably possessed fully evaginated cerebral hemispheres similar to those of *Protopterus* and *Lepidosiren*, for all modern amphibians, larval and adult,

exhibit this type of brain. The more diversified conditions of life on land appear to require far more complex centers of higher correlation than those possessed by any fish, and it seems probable that of all known forms of morphological pattern of the forebrain only that which possesses widely evaginated thin-walled cerebral hemispheres capable of indefinite expansion without undue thickening of the wall is adequate to form the foundation on which the complexity of higher brains could be elaborated.

Mention has been made of the high efficiency on the reflex plane of solid cerebral masses of teleostean type. In higher vertebrates with fully evaginated cerebral hemispheres local thickenings of a different sort appear in the lateral walls of the hemispheres themselves in reptiles and especially in birds. Here again this structural form is correlated with the predominance of stable, heritable, reflex and instinctive behavior patterns. In mammals, on the other hand, where individually modifiable behavior of the intelligent type is the most characteristic feature, so extensive solid thickenings of the walls of the hemispheres do not appear, but instead the highest correlation tissue of the brain is spread out in thin sheets as cerebral cortex (Kappers, '13, '14).

From a general survey of what is known regarding the correlation of forebrain patterns with behavior patterns, it appears that solid masses of cerebral tissue may be structurally well adapted for the performance of the most complex types of reflex and instinctive activity whose patterns are inherited and relatively stable, as illustrated in teleosts and birds. High specialization in this direction, however, seems to have precluded the possibility of any great development of the more labile individually modifiable sorts of behavior and especially of the culmination of this kind of behavior as manifested by capacity for rapid learning by individual experience and intelligence in general.

Conversely, the development of the labile functional type goes hand in hand with the extensive elaboration of thin sheets of correlation tissue, as exemplified in the cerebral cortex, in

which numerous functionally distinct fields are well separated in space and are at the same time in free communication through systems of association fibers of unlimited complexity, which find ample room in the subcortical white matter. There is no assignable limit to which structural specialization of this sort can extend. The nutritive requirements of the tissue are readily satisfied by its superficial position in close apposition with the rich blood vascular supply of the pia mater and with the cerebrospinal fluid of the meningeal spaces.

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